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Title of Thesis – Titre de la thèse

Temporal Processing Deficit in Glaucoma and Ocular Hypertension

Degree for which thesis was presented
Grade pour lequel cette thèse fut présentée
Ph.D.

Year this degree conferred
Année d'obtention de ce grade
1985

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Temporal Processing Deficit in Glaucoma and Ocular Hypertension

by

Lew Bohdan Stelmach

A Thesis
Submitted to the Faculty of Graduate Studies and Research in Partial Fulfilment of the Requirements for the Degree of Ph.D. in Psychology

Department of Psychology

Edmonton, Alberta
Fall, 1985

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THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

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Abstract

A two-pulse resolution technique was employed to assess temporal processing deficits in glaucoma and ocular hypertension. The first experiment showed that glaucomatous eyes were impaired at two-pulse resolution and that the severity of impairment was not uniform across retinal locations tested. Experiment 2 extended the investigation to a sample of hypertensive eyes and also examined a larger sample of glaucomatous eyes. A fair degree of separation was achieved between clinical and control samples. It was suggested that the severity of impairment in two-pulse resolution may be related to the amount of diffuse damage to the retinal nerve fiber layer.

Three ancillary experiments are reported. In one it was shown that impaired two-pulse resolution in glaucomatous eyes was not an artefact resulting from diminished light sensitivity. Another experiment replicated results of earlier work with patients suffering from multiple sclerosis and suggested that the current technique can be regarded as a valid measure of two-pulse resolution. The last experiment reports some anomalous data.

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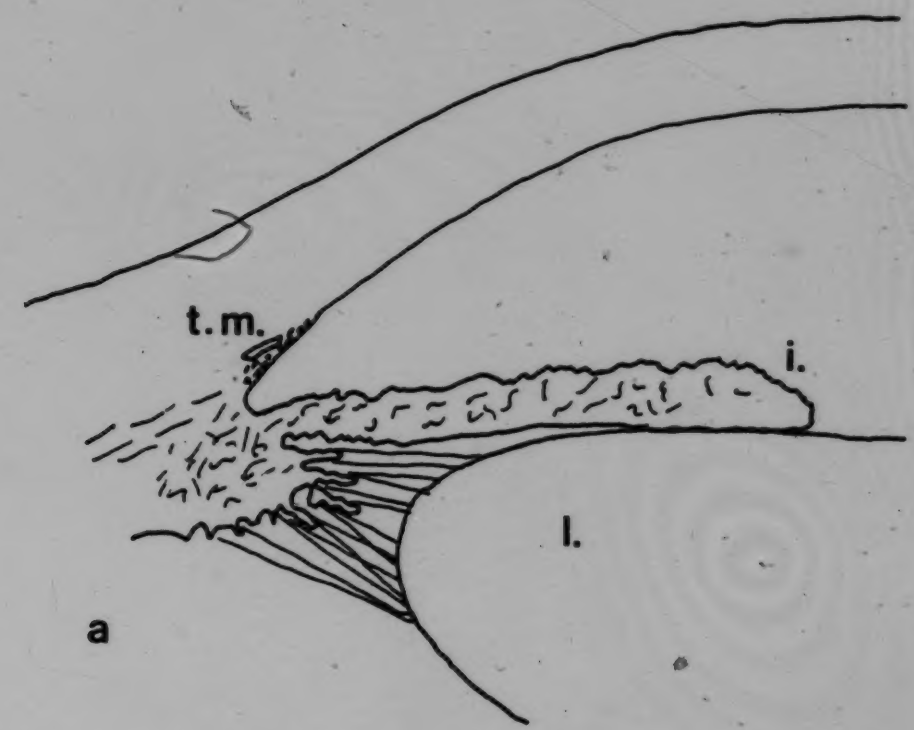
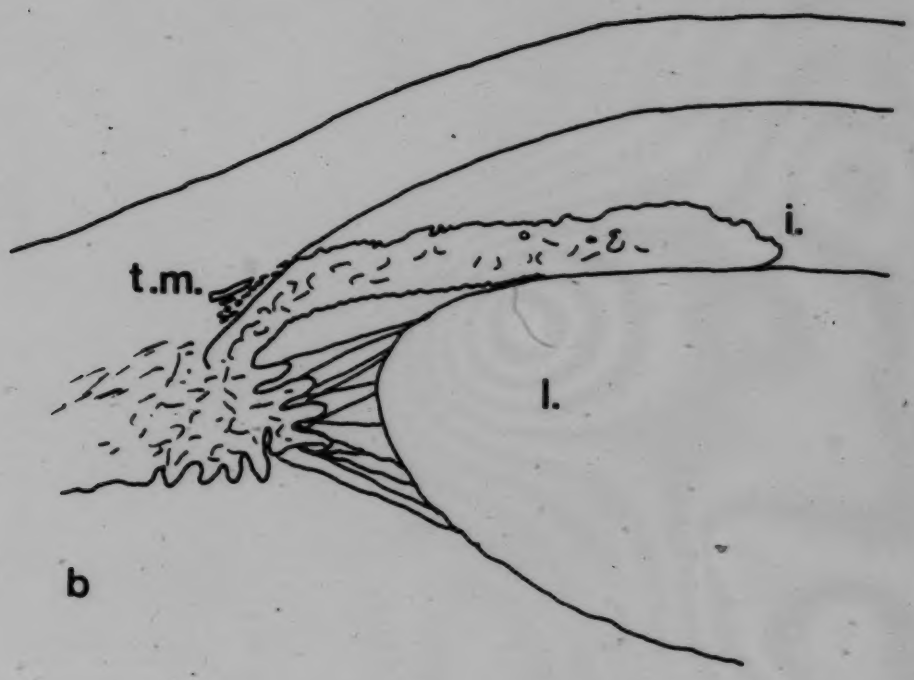
Simple chronic glaucoma, also termed open-angle glaucoma (OAG), is a condition of the eye in which elevated intra-ocular pressure is associated with deformation of the optic disc, deterioration of optic nerve fibers (axons of ganglion cells), and vision-loss. Normally, intraocular pressure is controlled by the ciliary body which excretes fluid (aqueous humor) into the anterior chamber of the eye and by the trabechular meshwork and canal of Schlem which release the fluid into the venous system. In glaucomatous eyes fluid pressure builds up due to blockage of the outflow system. In closed angle glaucoma, or acute glaucoma, the outflow system is mechanically blocked by a narrowing of the angle (see Figure 1). That is, the iris covers the trabechular meshwork and obstructs outflow. Intraocular pressure rises suddenly and is accompanied by pain and reddening of the eye (Simmons and Dallow, 1984). Provided that the patient seeks medical treatment, diagnosis and treatment of closed angle glaucoma is routine. By contrast, it is much more difficult to diagnose and treat open-angle glaucoma (OAG) where the trabechular meshwork is exposed to

Figure 1. Schematic representation of the anterior chamber of the eye. The angle between the iris and the trabechular meshwork is open in (a) and closed in (b); (t.m. - trabechular meshwork; i. - iris; l. - lens).



a



b

the flow of humor. Pressure build-up occurs because the outflow system becomes less permeable. It is believed that the change in permeability occurs at the point where the trabechular meshwork drains into the Canal of Schlem (Schwartz, 1984). The experience of OAG can be painless, explaining why it can go undetected for many years. The ultimate result of elevated intraocular pressure is degeneration of retinal axons and ganglion cells followed by vision loss. The research described here deals with open-angle glaucoma.

It is important to distinguish between two diagnostic categories: ocular hypertension and open-angle glaucoma. An individual is said to have ocular hypertension (OHT) when the angles are open, intraocular pressure is above 21 millimeters of mercury, the optic nerve head is not deformed and there is no vision loss. When visual field defects develop, or when cupping at the nerve head is detected, an individual is said to have open-angle glaucoma. Intermediate states may warrant the label of suspected OAG or early OAG.

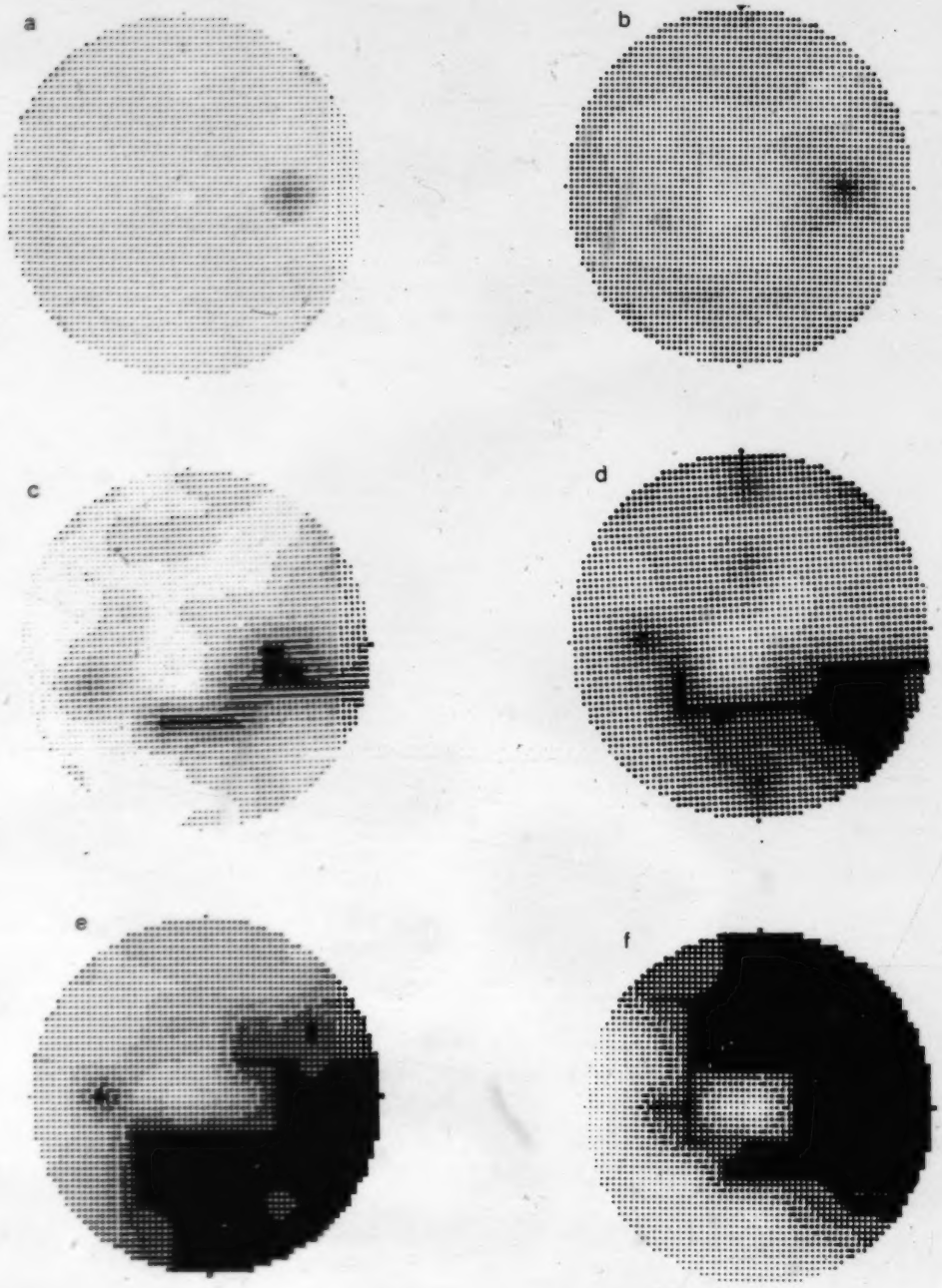
The sequence of events that leads from elevated intraocular pressure (IOP) to loss of vision is not fully understood. It is believed that elevated IOP increases the

wall tension of the sclera and distorts the lamina cribrosa. Since the optic nerve passes through the lamina cribrosa this compresses the nerve and its nutrient capillaries leading to axonal degeneration. (Anderson and Hendrickson, 1974; Leydhecker, 1983; Quigley, Addick, Green, and Maumenee, 1981;

Quigley et al (1981) studied the effects of elevated IOP on the axons at the point where they pass through the lamina cribrosa by inducing elevated IOP in nonhuman primates, and by examining human eyes postmortem. Both lines of investigation showed that elevated IOP caused intracellular matter to accumulate within the axons at the lamina, suggesting that axonal transport or normal axonal metabolism had been blocked. According to this analysis, one way in which elevated IOP causes loss of vision is by depriving axons of their nutrients.

Figure 2 shows progressive stages of vision-loss in different patients suffering from elevated IOP, as measured by static perimetry. This technique estimates relative threshold values of small flashes of light throughout the visual field. The threshold values are compared to mean values from a normal population and sensitivity maps are

Figure 2. Sensitivity maps showing the progressive deterioration of the perimetric fields in glaucomatous eyes. Panels (a) and (b) were obtained from right eyes; panels (c) - (f) from left eyes. The maps do not represent one patient.


a
b
c
d
e
f

generated showing deviations from normality. Each map in Figure 2 represents sensitivity over 60 degrees of the visual field. Severity of loss is indicated by the amount of shading. Solid black indicates a scotoma. Figure 2(a) shows a normal visual field. The dark patch in Figure 2(a) represents the blind spot. Figure 2(b) through 2(f) show visual fields with progressively larger scotomata.

As can be seen from Figure 2, deterioration appears first in peripheral and paracentral vision. As measured by static perimetry, foveal vision can remain normal until late stages of glaucoma. An example of this is shown in Figure 2(f).

Deficits in visual function, as measured by static perimetry, can be preceeded by fairly extensive damage to the optic nerve. That is, a patient may have apparently normal visual fields, yet have a definite loss of axons. In most cases this loss would appear as an enlargement of the optic disk cup (Drance, 1984; Quigley, Addick and Green, 1982; Quigley, 1983). For example, postmortem examination of five eyes suspected of having glaucoma, but with normal perimetric fields, revealed that three of these eyes had a mean loss of 37% of their axons. That is, the optic nerve containes about

600,000 fibers rather than the normal 1,000,000, yet visual function was normal, as assessed by perimetry (Quigley, et al, 1982).

The challenge for psychophysics has been to devise new tests which might be sensitive to early damage to the retina and optic nerve resulting from elevated IOP. Discerning such early abnormalities may eventually permit the systematic detection and treatment of subclinical visual changes prior to the development of scotomata (Atkin, Podos & Bodis-Wollner, 1983). To date,psychophysical investigations have shown that ocular hypertensive patients are likely to have poor blue-yellow and blue-green color discrimination (Drance, Lakowski, Schulzer & Douglas, 1981; Fishman, Krill & Fishman, 1974; Lakowski, Bryett, Drance, 1972;), contrast sensitivity losses (Bodis-Wollner and Camisa, 1980; Ross, Bron & Clarke, 1984), receptive field abnormalities (Enoch and Lawrence, 1975; Enoch and Campos, 1979) and flicker sensitivity losses (Atkin, Bodis-Wollner, Wolkstein, Moss, Podos, 1979; Tyler, 1981). So far it is still premature to judge which of the foregoing approaches will have the best prognostic value or which will gain clinical acceptance. However, methods which assess temporal functioning, such as flicker threshold techniques, seem particularly promising.

Deficits in flicker sensitivity have been demonstrated by Atkin et al (1979) in two separate tasks. The first task measured the threshold contrast for perception of 8 Hz flicker of a homogeneous circular display subtending 4 degrees of arc. The second task measured threshold contrast for perception of a sinusoidal pattern of vertically aligned dark and light bars as it flickered in counterphase at 8 Hz. Atkin et al. did not report the results for each task separately. Rather, they computed for each subject a combined average score called DRC (dynamic response coefficient). Half of the eyes without perimetric field defects were judged to be abnormal by this method, whereas, all but one of the eyes with parafoveal visual field defects were judged to be abnormal (Atkin et al 1979). This pattern of results were replicated by Atkin, Bodis-Wollner, Podos, Wolkstein, Mylin & Nitzberg (1983).

Sensitivity of a test for detecting early damage to the retina and optic nerve can be assessed by noting the percentage of ocular hypertensive patients who are judged abnormal. These patients have elevated IOP, normal optic discs and normal visual fields. The accepted criterion for abnormality typically permits a 1% false alarm rate. That is,

1 in 100 patients with normal IOP and normal visual fields might be classified as abnormal erroneously. The method developed by Atkin and associates, described above, has a sensitivity of about 50% because about half of the patients with OHT were classified as abnormal.

A psychophysical test which detects about 90% of ocular hypertensive patients has been reported by Tyler (1981). Tyler's method was similar to the first task employed by Atkin et al (1979, 1983) where observers were required to detect flicker in a spatially homogeneous field. The critical difference between the two was that Tyler varied the temporal frequency or flicker rate of the display rather than holding it constant at 8Hz. Tyler found that 90% of patients exhibited significant losses in sensitivity at flicker rates of 30 - 40 Hz. A smaller percentage of patients were classified as abnormal at frequencies above and below this range. At 5 - 10 Hz the proportion of patients classified as abnormal was approximately equal to that reported at 8 Hz by Atkin et al (1979). To date, Tyler's method has shown the greatest sensitivity to early damage resulting from elevated IOP. But note that the clinical value of a particular method is determined as much by prognostic value as by diagnostic

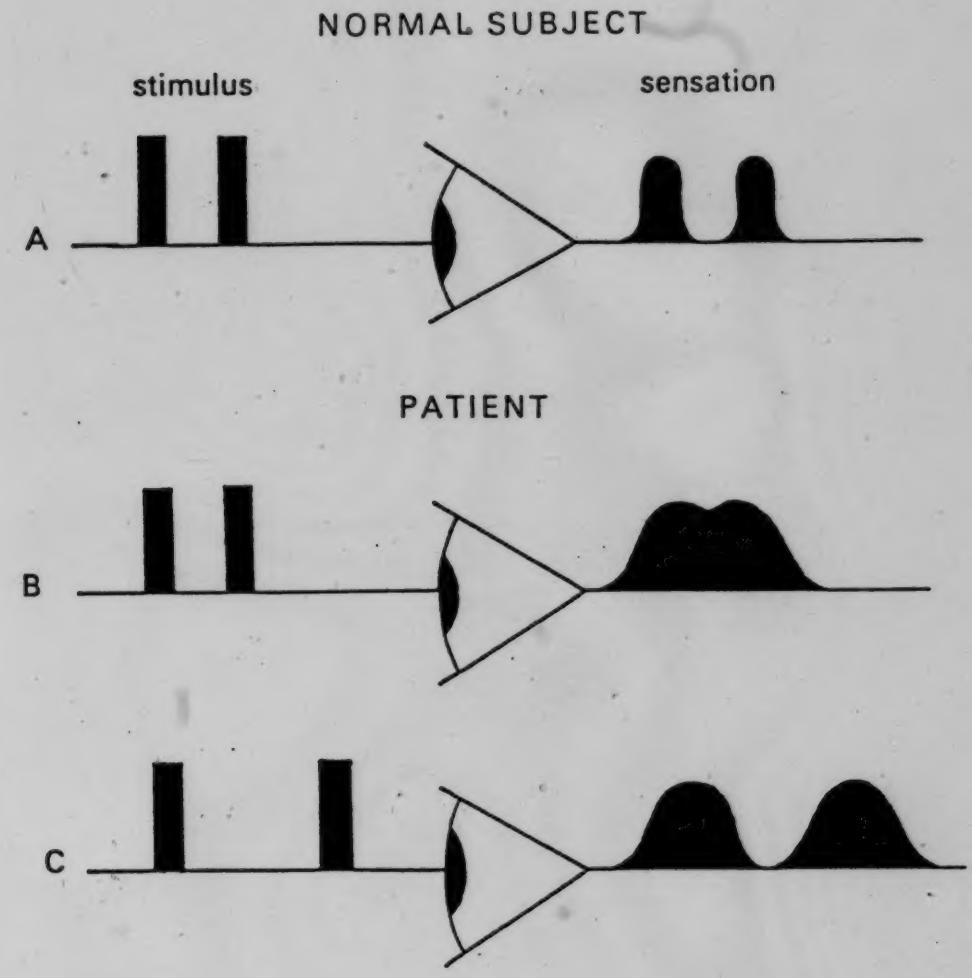
yield. Only longitudinal studies which follow a sample of patients for a number of years can discover whether patients with poor scores on a given test are the same ones who will progress and develop field defects.

Losses in flicker sensitivity or, in general, deficits in processing stimuli which vary in time are not specific to glaucoma or ocular hypertension. Similar deficits have been demonstrated in patients suffering from other disorders, for example multiple sclerosis (Daley, Swank & Ellison, 1973; Galvin, Regan & Heron, 1976; Galvin, Heron & Regan, 1977; Parsons & Miller, 1957; Mustillo, Brussell, White & Anderson, 1984) and dyslexia (Di Lollo, Hanson & McIntyre, 1983). A technique which has proven to be particularly effective in detecting temporal processing deficits in these clinical populations has been the two-pulse resolution method (Galvin et al., 1976; Di Lollo et al., 1983). Observers are shown two pulses of light in rapid succession to the same area of retina. The technique measures the duration of the interval between the two pulses at which the observer reports a perception of "double flash". Glavin et al. (1976) and Di Lollo et al. (1983) report that the clinical populations in their studies required longer intervals between the pulses to perceive two flashes than did control observers.

The rationale for using two-flash discrimination to study deficits in temporal processing is illustrated in Figure 3 (adapted from Galvin et al, 1976). A double flash might appear as a single flash to an observer with impaired vision because the responses to each flash merge. That is, the second flash is presented before the visual system has recovered from the effects of the first flash (Figure 3b). Consequently, a longer ISI is required to restore the perception of "double flash" (Figure 3c). By measuring the probability of seeing a double flash at various durations of ISI it is possible to quantify the severity of impairment of patients relative to controls. However, care must be taken to eliminate extraneous cues, such as brightness and duration, which might identify a double flash target, even when a double flash is not perceived.

A systematic investigation of two-pulse resolution thresholds in patients suffering from elevated IOP or glaucoma has not been reported in the literature. However, a preliminary investigation by Galvin et al (1976) reported some encouraging results: 10 of 14 eyes with elevated IOP had abnormal two-pulse resolution thresholds. However, 7 of these eyes may have been in advanced stages of the disease. In

Figure 3. Schematic representation of the two-pulse target and the resulting sensations in normal and impaired observers. Adapted from Galvin, Regan and Heron, 1976.


NORMAL SUBJECT
stimulus
sensation
A
PATIENT
B
C

order to assess the sensitivity of the two-pulse resolution method to early damage resulting from elevated IOP the present work reports data collected from three populations: normal, ocular hypertensive - OHT (elevated IOP with no visual field defects), and glaucomatous (elevated IOP with visual field defects). It is hoped that the two pulse method will provide valuable diagnostic information about early signs of damage at retinal locations which appear normal by inspection and have normal perimetric fields.

Experiment 1

The goal of Experiment 1 was to ascertain whether the two-pulse resolution method could discriminate between glaucomatous patients with parafoveal perimetric field defects and control observers with no known visual defects.

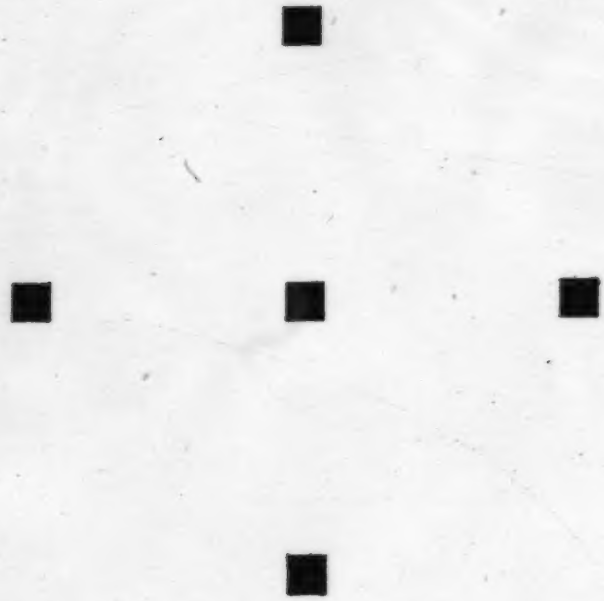
Psychophysical investigations of visual dysfunction typically utilize the "yes-no" response procedure. The observer responds "yes" if he can detect the relevant feature of the display, or "no" if he cannot. This procedure is preferred primarily for its speed. However, the "yes-no" procedure has a serious drawback: each observers must set up a response criterion. Given a conservative criterion and some degree of uncertainty, the observer will tend to respond "no". Alternatively, a liberal criterion will produce more "yes" responses. In either case, sensory effects and response criterion effects will be confounded. Shortcomings of the "yes-no" procedure in clinical testing have been discussed at length by Vaegan and Halliday (1982). As an alternative, they recommend the forced-choice procedure which is virtually criterion free. In a forced-choice procedure the event of interest occurs on every trial. Thus, there is

no uncertainty as to its presence. Observers are required merely to indicate where or when it occurred. Advantages of the forced-choice procedure have been recognized in nonclinical applications as well (Sharf, 1975; Stelmach, Bourassa and Di Lollo, 1984). To minimize biases introduced by observers' response criteria the present research adopted a forced-choice procedure.

There were two tasks in Experiment 1. In one task five elements were displayed in the configuration shown in Figure 4. On each trial, all elements were shown in one pulse, except for one element which was shown in two pulses separated by a temporal gap. Observers were required to name the location of the two-pulse element. On the hypothesis that glaucomatous patients have a temporal processing deficit they should require a longer interpulse interval to identify the location of the two-pulse target with the same degree of accuracy as controls.

In the second task the display configuration was unchanged. However, on each trial the observer viewed the display twice. In one of the two display intervals, all five elements were presented in a single pulse. In the other interval all elements were presented in a single pulse except

Figure 4. Display elements were arranged as shown here. In Experiments 1 and 5 the distance of the outer elements from the center was either 2, 3 or 4 degrees of visual angle. In Experiments 2, 3 and 4 it was 3 degrees.



for one which was presented in two sequential pulses. Observers were required to identify which interval (first or second) contained the two-pulse element, but were not required to name its location. The second task was introduced as an exploratory measure because it may have interesting implications regarding the relationship between spatial and temporal visual functioning. It also would be valuable to know whether patients and controls observers differed in this respect.

Method

Subjects. Testing involved many trials (6000 or more per subject) therefore, only two glaucomatous patients (MT and AG) and three controls (VDL, JMF and WS) served in the experiment. One eye of each observer was tested (left eye of AG, VDL and JMF; right eye of MT and WS). All tested eyes had normal or corrected-to-normal Snellen acuity. Patients MT and AG were 62 and 61 years of age, respectively. Controls VDL, JMF and WS were 54, 56 and 56 years of age, respectively.

All five participants had no history of neurological disorders. Control eyes had normal visual fields and no history of eye disease. Glaucomatous eyes had paracentral visual field defects and no scotomata within a radius of 4 degrees from fixation.

Pupil size of the tested eyes measured at a background luminance of approximately 8.6 cd/m^2 was 3.25 mm and 4 mm for MT and AG, respectively, and 6 mm for VDL, JMF and WS, respectively.

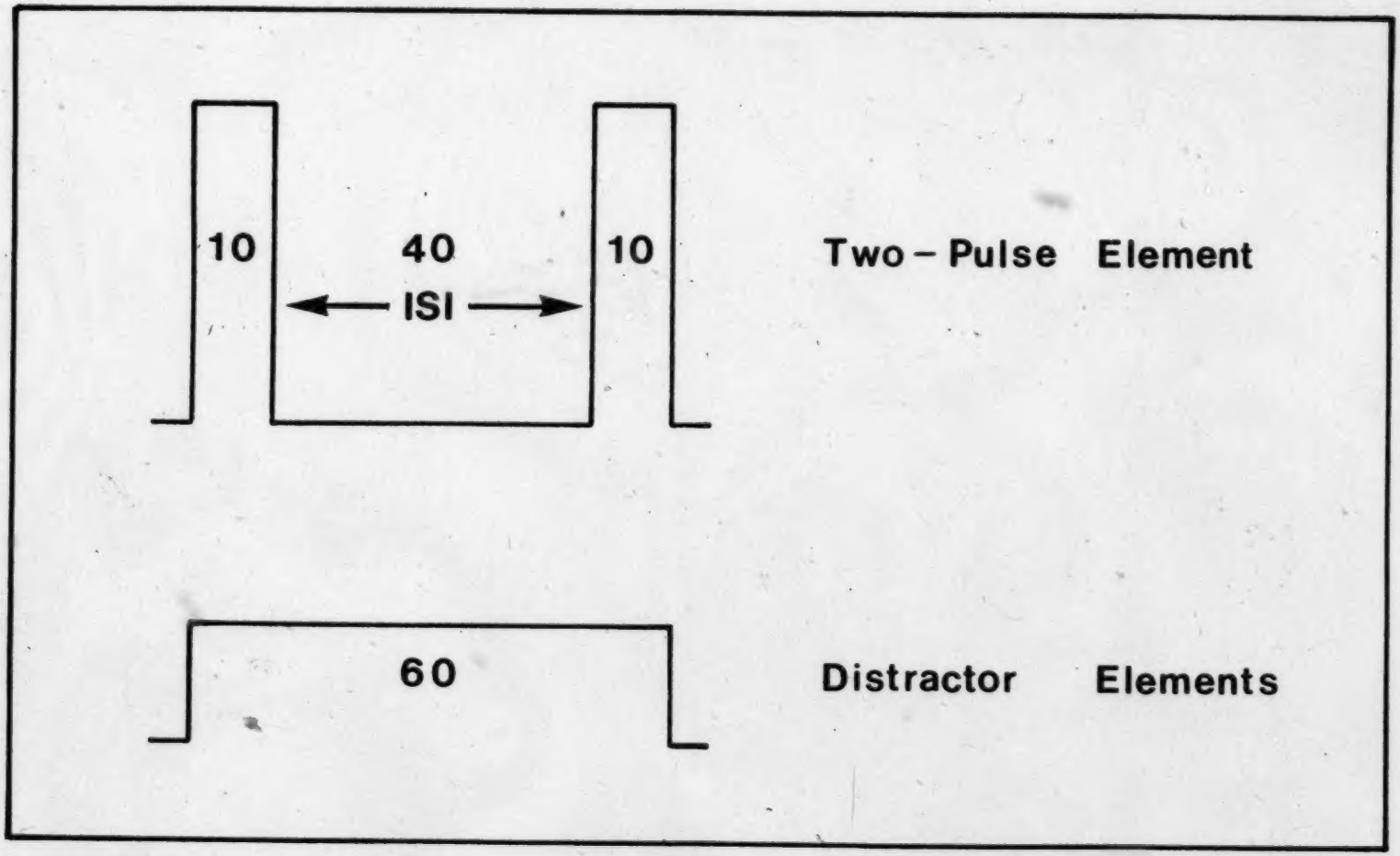
Intraocular pressure (IOP) measured in millimeters of mercury with applanation tonometry ranged from 14mm Hg to 32mm Hg for MT and from 13mm Hg to 18mm Hg for AG. Elevated pressures were being treated with Carbachol and Tymolol for

MT, and with propine for AG. Control observers VDL, JMF and WS had IOPs of 15mm Hg.

Display Characteristics. The display consisted of five square elements, arranged as shown in Figure 4. Each element was composed of 9 dots arranged in 3 x 3 matrix. The central element was always displayed at the fixation point. The four outer elements were positioned at a distance of either 2, 3, or 4 degrees from fixation. On any given trial all four outer elements were positioned at the same eccentricity. At a viewing distance of 57 cm which was set by a headrest, each element subtended a visual angle of approximately 20 minutes of arc.

On each trial, one of the five elements, chosen randomly, was designated as the target. This element was displayed in two separate flashes of 10 ms each, separated by a variable interval (ISI). The remaining four elements (the distractors) were displayed for the same duration as the target, but without an ISI. For example, if the ISI were 40 ms the total duration of the target element would be 60 ms: the ISI plus the two 10 ms pulses. In this case, the distractor elements also would be displayed for 60 ms (Figure 5).

Figure 5. Schematic representation of the temporal relationship between the two-pulse target and the distractors. The duration of each pulse in the two-pulse element was always 10 ms. The duration of the ISI varied, as did the duration of the distractors. This figure illustrates a case in which the duration of the ISI was 40 ms and the duration of the distractors was 60 ms. The important point is that the duration of the distractors was always equal to the total duration of the two-pulse element: 20 ms plus the duration of the ISI. Note also that the integrated light energy in the two-pulse element and in the distractor element is the same, indicating equal brightness.


10
40
ISI
10
Two – Pulse Element
60
Distractor Elements

Displays were shown on a Hewlett-Packard 1333A oscilloscopic point plotter equipped with fast P15 phosphor. Background luminance was maintained at a mesopic level (8.6 cd/m^2 as measured with a Tektronix J16 photometer).

Controlling Bases of Judgment. Since the goal of the experiment was to estimate the detectability of the double flash, an effort was made to eliminate extraneous cues, such as duration and brightness which might idependently identify the two-flash target (Kietzman and Sutton, 1968). If the duration of the target and distractors were unmatched, or if the target differed from the distractors in terms of brightness, observers could detect the target even if a double pulse were not visible. In either case, the results would not reflect observers' ability to perceive a double flash, but would be contaminated by responses based on irrelevant dimensions of the display. In order to avoid this problem the duration and brightness of target and distractor elements was matched, so that the target element did not differ from the distractor elements in terms of duration or brightness. Matching duration was simple: as described above, on any given trial the duration of the distractors was set to the the total duration of the target element: ISI plus

20 ms. Matching brightness was less simple: the luminance of the target and distractors was adjusted until their brightness appeared to match that of a standard element. The standard was displayed 2.5 log units above threshold for 100 ms with no ISI. The matching procedure had a number of steps. First, the two-pulse elements were matched in terms of brightness with the standard. Second, the distractors were matched in terms of brightness with their respective targets.

Next, to limit the effect of any residual mismatch in brightness between target and distractors, a slight variation was introduced in the brightness of the distractors, encompassing the brightness of the target element. Finally, the new matched values were validated in a separate procedure where observers attempted to discriminate the target from the distractors on the basis of brightness alone.

The primary result of the matching procedure was that targets and distractors were of approximately equal brightness. However, an additional effect of the matching procedure was that targets and distractors looked equally bright regardless of their duration. This aspect of the equalization procedure was aimed at controlling brightness as

a variable which might affect performance on the two-pulse task (Onley and Boynton, 1962).

Design and Procedures. Observers sat facing the oscilloscope's screen in a sound-attenuated room. Background luminance was maintained at a constant value of 8.6 cd/m^2 measured by a Tektronix J16 photometer at the blank surface of the oscilloscope's screen.

There were two tasks in Experiment 1. Both used the display described above, but used different procedures.

Task I: Position-bound task. In this task observers were required to name the position of the two-pulse element. The sequence of events on each trial was as follows: The observer fixated the center of a square area defined by four dots. These were located a short distance beyond the corners of the central element. Remember that no elements were visible while fixation was on. When ready, the observer pressed a button. The fixation dots disappeared and the five elements were displayed. The observer then responded by naming the location of the two-flash target (top, bottom, left, right, or center). The experimenter entered the response on a keyboard and the next trial commenced.

Task II: Position-free task. In the position free task each trial consisted of two display intervals. A two-pulse target was presented only in one interval and, as above, only at one location. The sequence of events on each trial was as follows: The observer fixated the center of the area defined by the four fixation dots. When ready, the observer pressed a button to initiate the first display. The fixation dots disappeared and five elements were displayed. Immediately following this display, the fixation dots reappeared and the observer pressed the button again to initiate the second display. After viewing both displays, the observer responded by naming the display interval (first or second) in which a blink or double-flash was seen. Observers were not required to name the position of the target.

Patients and controls were tested on both position-free and position-bound tasks. On each task, three eccentricities were tested: 2, 3 and 4 degree. Note, that on any given trial of either task, all four outer elements were always displayed at the same eccentricity. Since observers' ability to see a double flash could vary from one testing site to another, a range of ISIs was selected for each observer at each combination of task, position and eccentricity so that level of performance encompassed the 50% level. Within a

given session, the type of task and the eccentricity was held constant, while the position of the target and the duration of the ISI varied unpredictably. Each combination of position and duration of ISI was tested 5 times within a session (125 - 175 trials per session). Each subject served for eight sessions at each combination of task and eccentricity, for a total of 40 observations per data point. A session lasted about 10 minutes. There was a 3 - 5 minute rest period between sessions, and a 10-minute rest period every two sessions. Subjects completed 4 - 6 sessions per day. Trials were randomized within a session, and sessions were randomized across days. All scoring, timing and display functions were performed by a PDP-11/34A computer.

Figure 6. Percentage of correct responses in the position-bound task, separately for each observer in Experiment 1. Data have been averaged over all three eccentricities and over the outer positions in the display. Open symbols represent normal eyes. Filled symbols represent glaucomatous eyes.

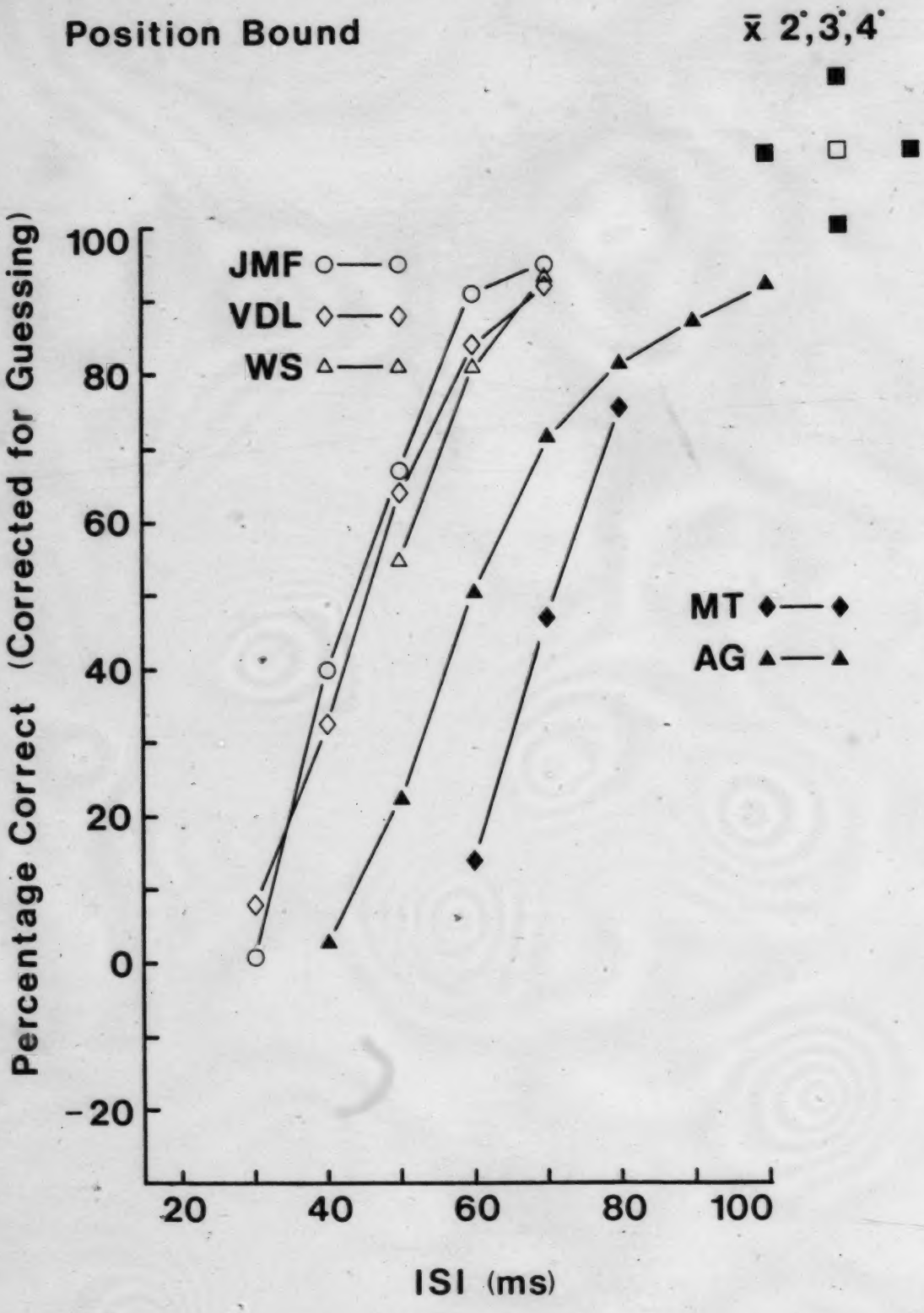

Position Bound
x̄ 2',3',4'
JMF
VDL
WS
MT
AG
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)

Figure 7. Percentage of correct responses in the position-free task, separately for each observer in Experiment 1. Data have been averaged over all three eccentricities and over the outer positions in the display. Open symbols represent normal eyes. Filled symbols represent glaucomatous eyes.

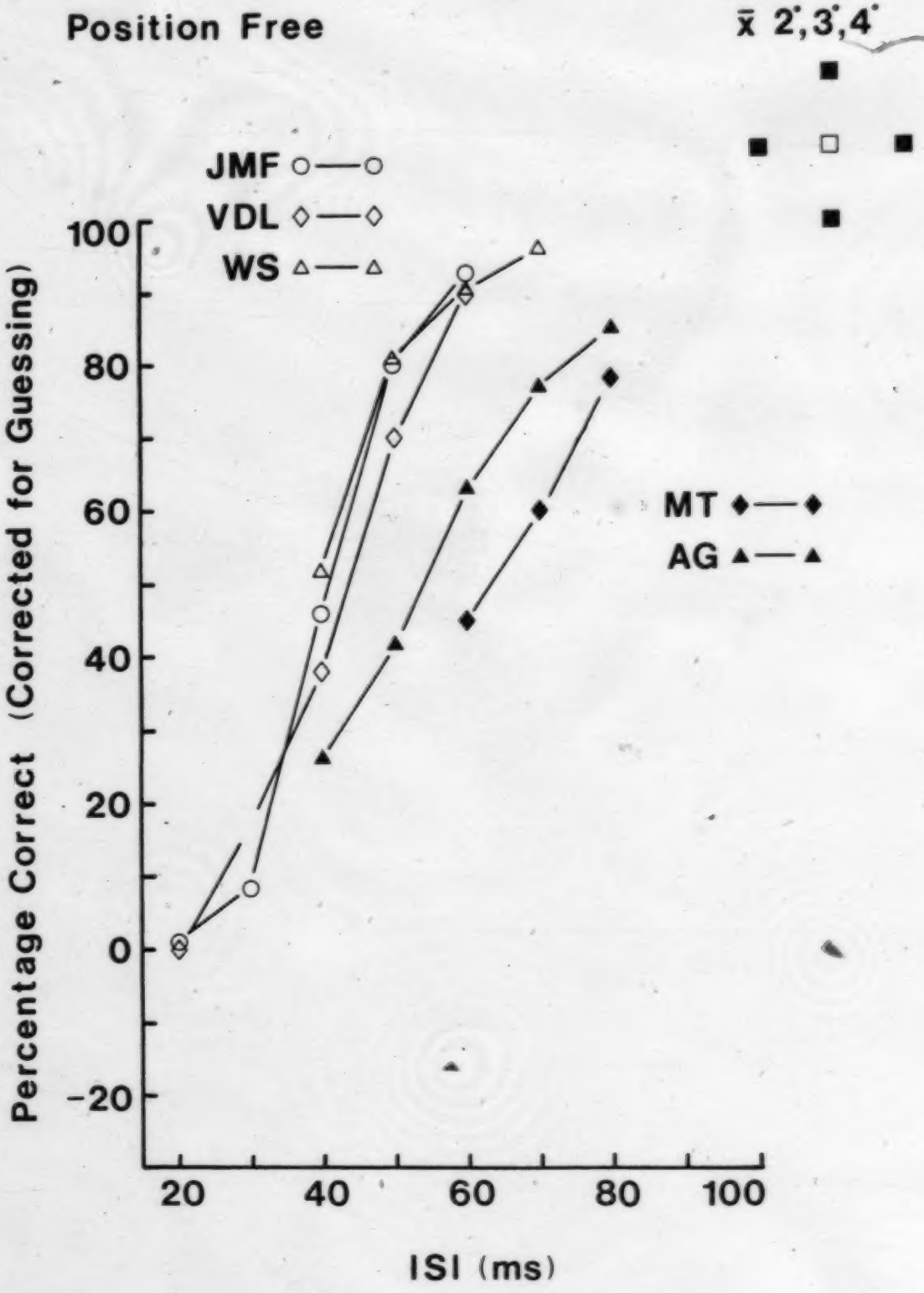

Position Free
x̄ 2°,3°,4°
JMF
VDL
WS
MT
AG
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)

Figure 8. Percentage of correct responses showing the difference between the position-bound and position-free tasks in Experiment 1. Data have been averaged over glaucomatous observers (open symbols) and over normal observers (filled symbols).

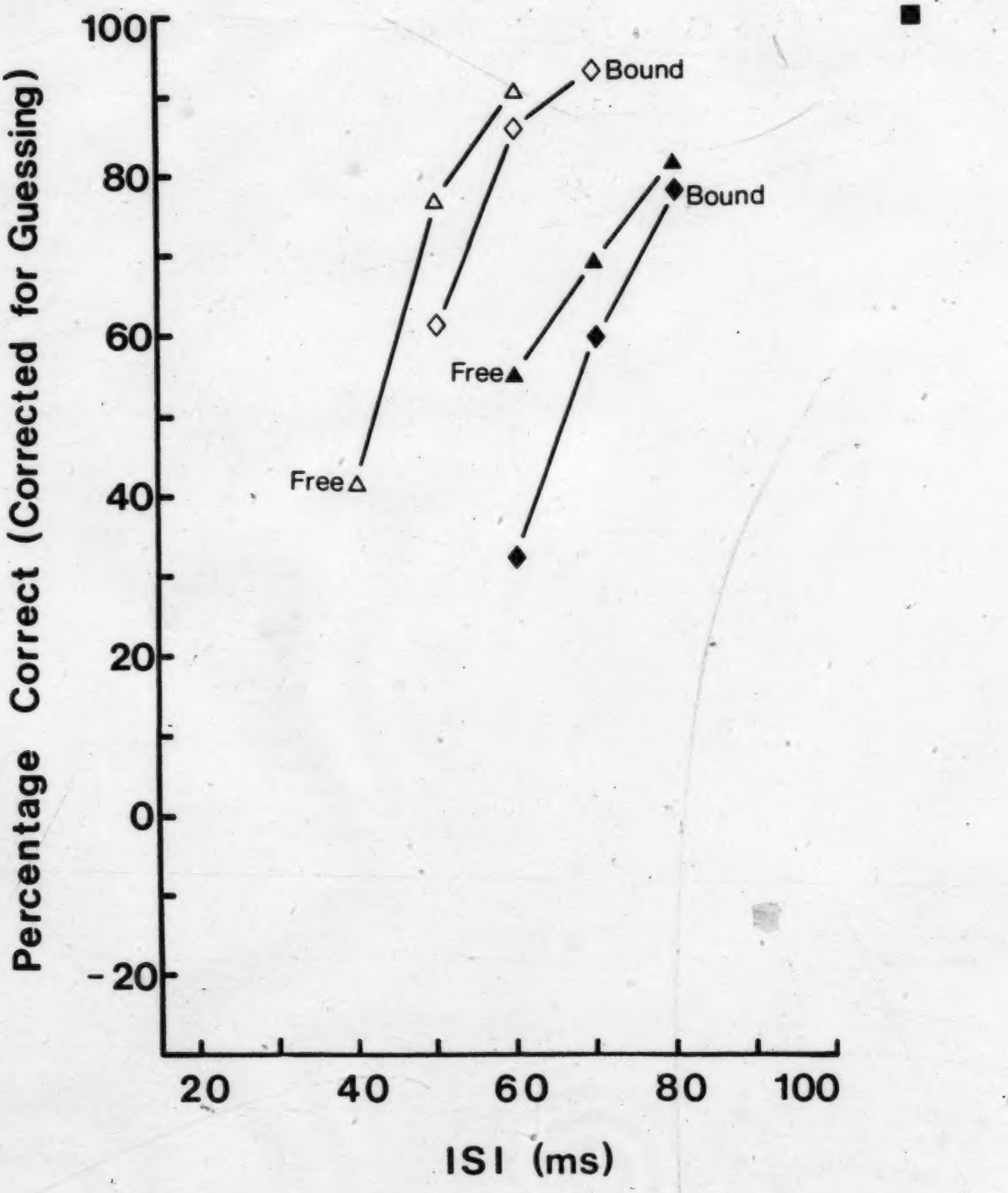

x̄ 2',3',4'
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
Bound
Bound
Free
Free

Figure 9. Percentage of correct responses for observer JMF separately at each of the four outer display locations at an eccentricity of 3 degrees.

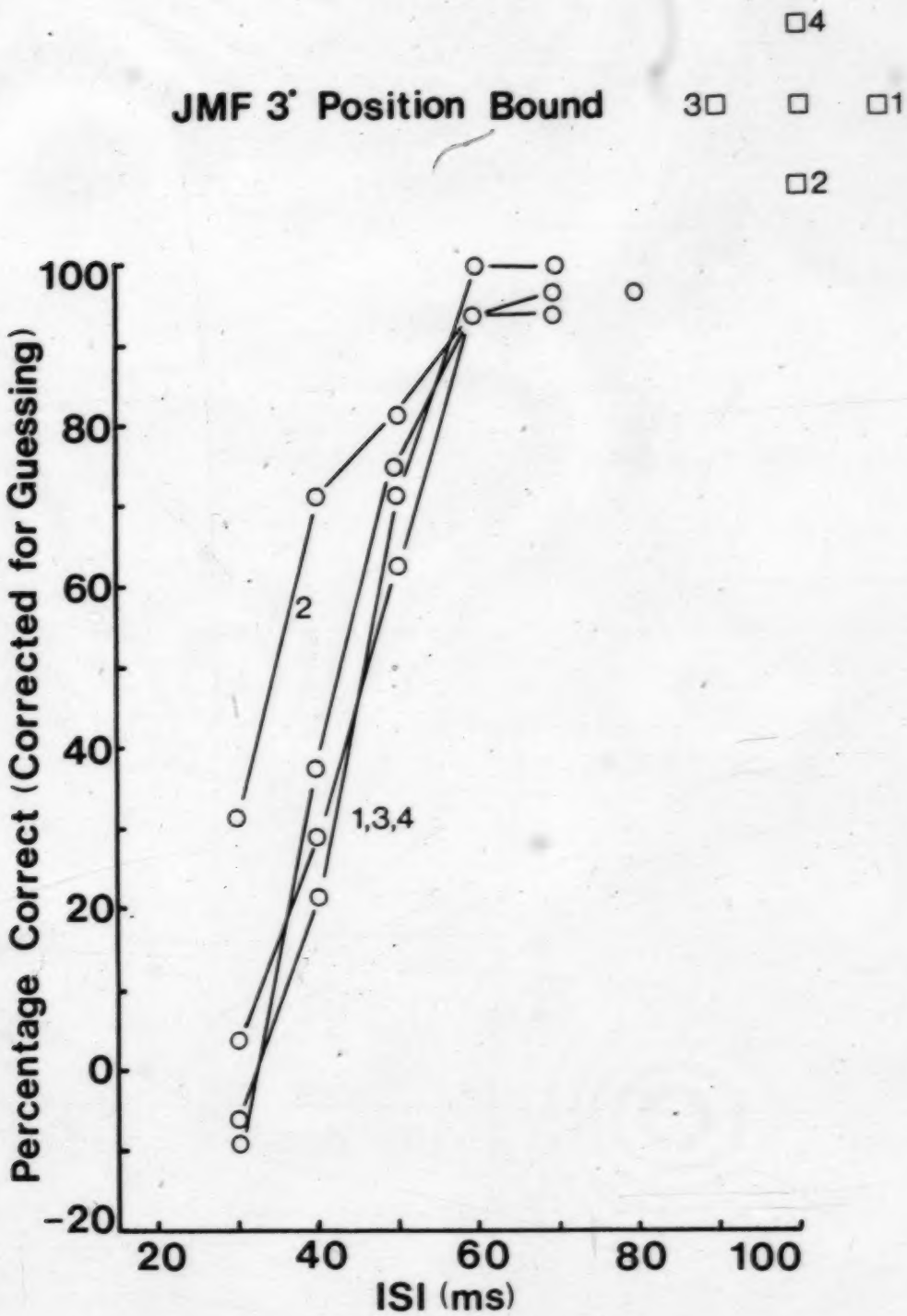

JMF 3° Position Bound
□4
3□
□
□1
□2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
2
1,3,4

Figure 10. Percentage of correct responses for observer VDL separately at each of the four outer display locations at an eccentricity of 3 degrees.

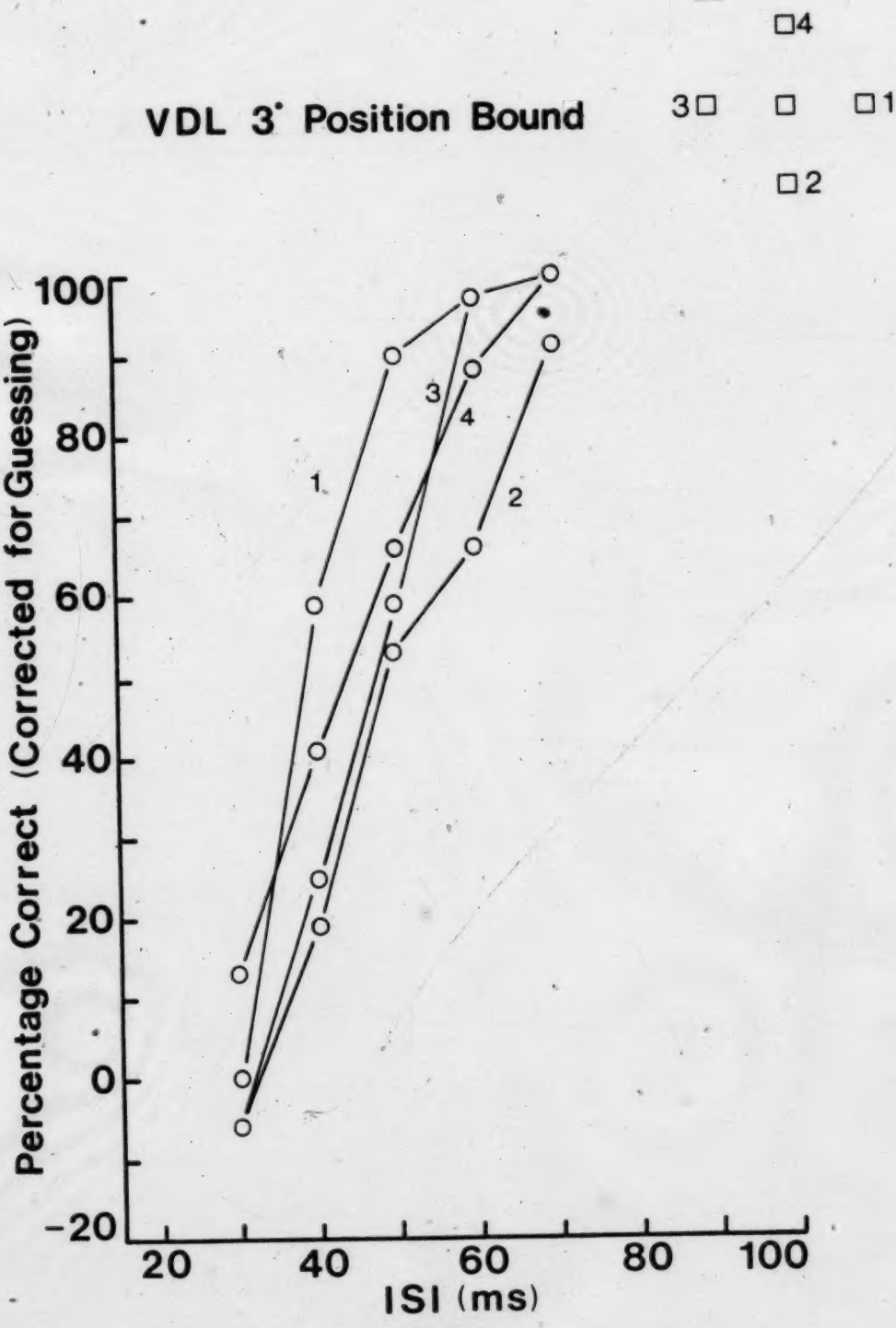

VDL 3° Position Bound
□4
3□ □ □1
□2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
1
2
3
4

Figure 11. Percentage of correct responses for observer WS separately at each of the four outer display locations at an eccentricity of 3 degrees.

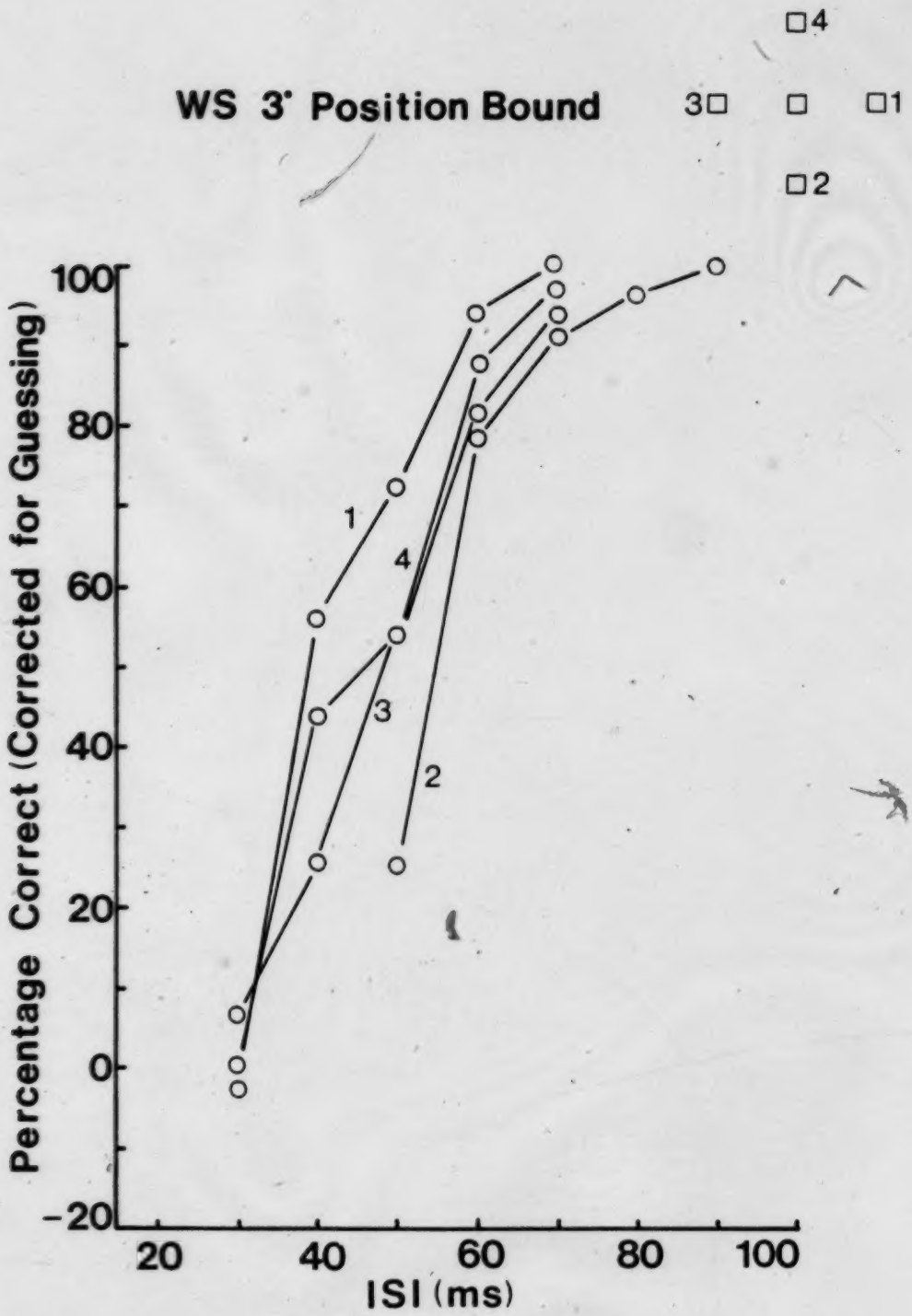

WS 3' Position Bound
□4
3□
□
□1
□2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
1
2
3
4

Figure 12. Percentage of correct responses for observer AG separately at each of the four outer display locations at an eccentricity of 3 degrees.

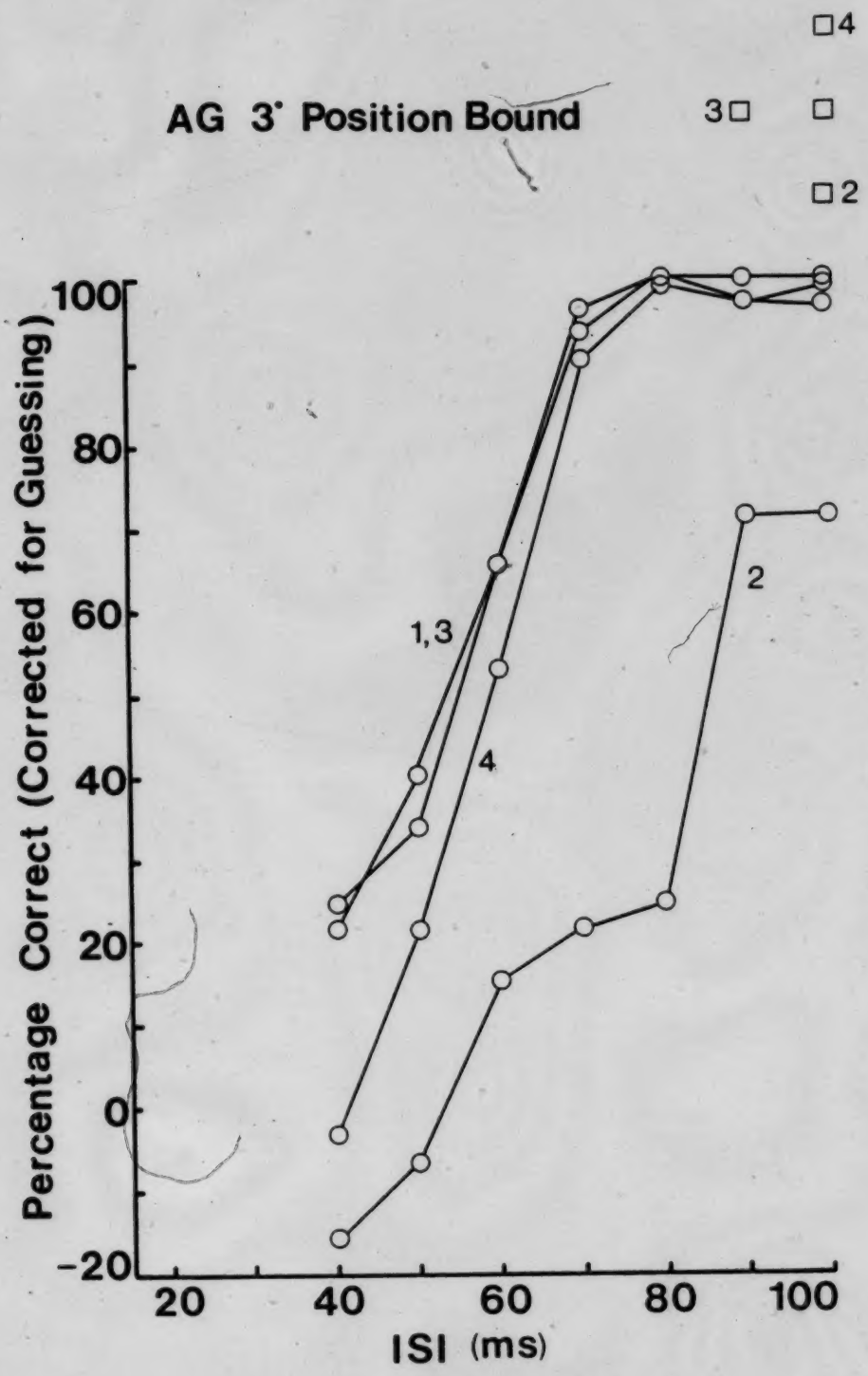
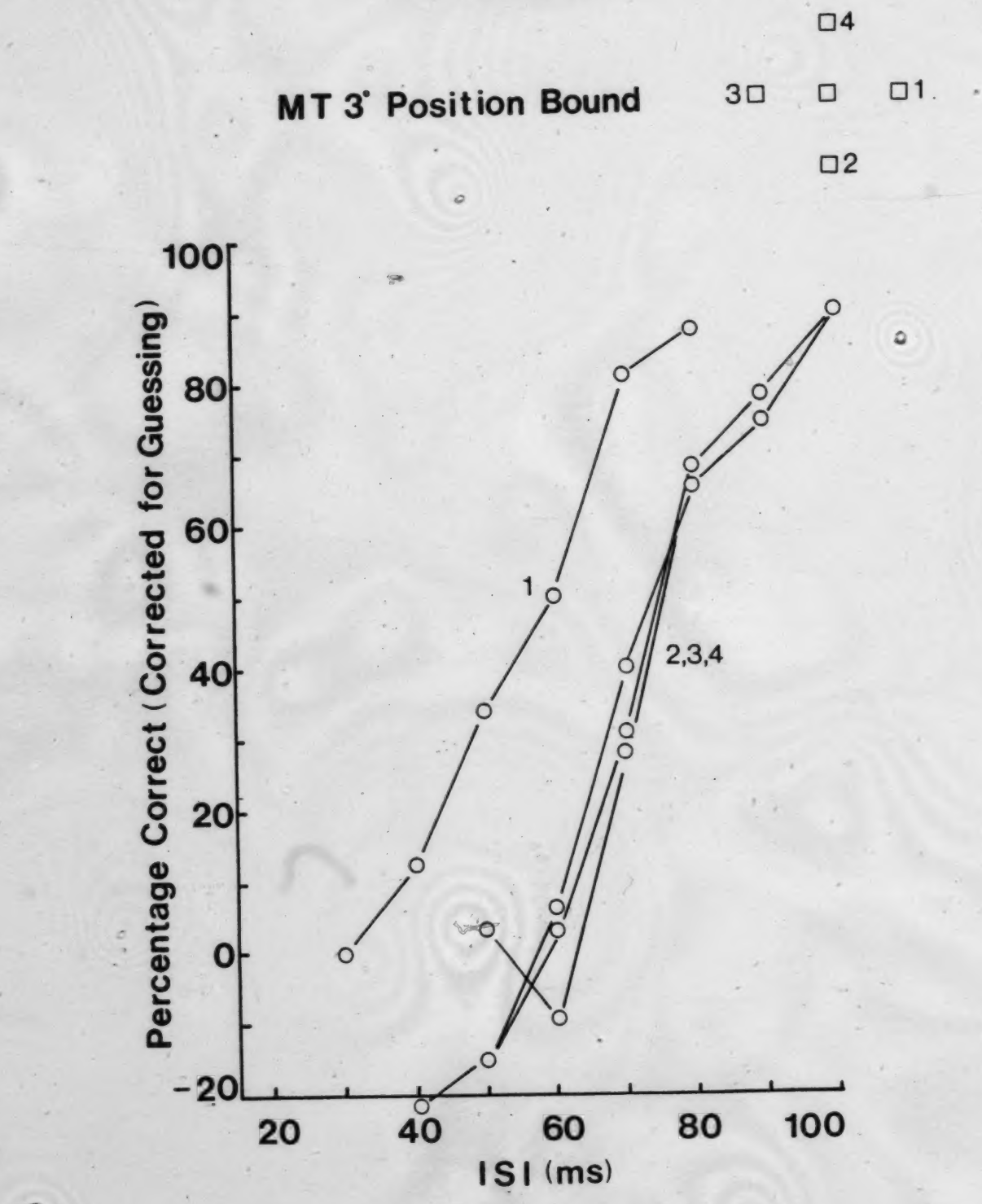

AG 3' Position Bound
4
3
1
2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
1,3
4
2

Figure 13. Percentage of correct responses for observer MT separately at each of the four outer display locations at an eccentricity of 3 degrees.


□4
MT 3° Position Bound
3□ □ □1
□2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
1
2,3,4

Results and Discussion

Results of Experiment 1 are presented in detail in Appendix A. Each table in the appendix show results of one observer on one task. Thus there are two tables per observer, and a total of 10 tables. The values in the body of each table indicate the percentage of correct responses adjusted for chance. In the position-bound task the probability of making a correct response by chance alone was 1/5, whereas in the position-free task it was 1/2. Observers' scores were adjusted for chance to enable direct comparisons between level of performance on both tasks. Adjusted scores reflect the degree to which performance exceeds chance-level responding.

The salient aspects of the results are presented graphically in Figures 6 through 13. Figures 6 and 7 show the results averaged over all positions of the display with the exception of the central position and averaged over all three eccentricities. Data are shown separately for each observer (open symbols for controls, filled symbols for patients). The rightward displacement of the filled symbols

relative to the open symbols indicates that patients required longer interstimulus intervals (ISIs) between the two pulses to attain the same level of performance as controls. This pattern was evident regardless of whether observers were required to identify the location of the pulsed target (Figure 6) or simply detect its presence (Figure 7). It should be noted that performance on the two tasks did not provide a basis for discriminating between patients and controls and, thus, disconfirmed the hypothesis that glaucomatous patients can perceive a double pulse, but have difficulty localizing it. Rather, both groups performed slightly better in the position-free task than in the position-bound task. This is shown in Figure 8, where the data have been averaged across observers. This difference is discussed later in the present dissertation.

Degree of impairment in temporal resolution exhibited by glaucomatous patients was not uniform at all retinal locations. Figures 9 through 13 illustrate for each observer how level of performance varied from one location to the next. The numbers (1-4) refer to the positions in the display shown at top right of each figure. Note the relationship between the curves within each figure. The

clustering of the curves of the control observers (VDL, JMF and WS) contrasts markedly with the wide spacing of the curves of glaucomatous observers (AG and MT). This pattern of results suggests that while control observers had relatively uniform temporal sensitivity at all locations tested, the temporal sensitivity of glaucomatous observers varied dramatically across locations. These results are in accord with the observation by Airaksinen, Drance, Douglas, Mawson and Nieminen (1984) that the distribution of damage to the retinal nerve fiber layer is not uniform. Variations in the degree of damage to the nerve fibers in the retina might account for the variability in temporal sensitivity across the retina exhibited by AG and MT.

In Figures 9 through 13 the intermediate eccentricity of 3 degrees was chosen for illustrative purposes; however, apart from an overall deterioration in performance with increasing eccentricity, the pattern of results at an eccentricity of 3 degrees is entirely represenattive of the remaining eccentricities. The rate of deterioration in performance with increasing eccentricity was similar for all observers except for AG whose performance deteriorated most rapidly. This may be suggestive of a difference between control and glaucomatous observers, however, given that MT

did not show this effect, the results do not permit a conclusive statement.

It should be noted that both MT and AG were able to see all stimuli in the display, yet were impaired in their ability to resolve two successive flashes. That is, at the locations tested, they had normal sensitivity to light, but abnormal temporal resolution. This was confirmed in an ancillary experiment, reported below as Experiment 3. Experiment 3 showed that the duration of the interpulse interval required to attain criterion level performance was not correlated with perceived brightness. Of course, this does not preclude the possibility that retinal locations exhibiting a temporal processing deficit might have additional deficits, say for example, in color or contrast sensitivity.

In summary, results of Experiment 1 showed that the two-pulse resolution test can discriminate between patients with parafoveal field defects and controls. As well, the results showed that visual damage can extend beyond retinal areas where perimetric field defects are known to exist providing evidence for diffuse damage of the retinal receptors or nerve fiber layer. In the next experiment a modified version of the test was applied to larger samples of

glaucomatous patients, control observers and a new group of ocular hypertensive patients.

Experiment 2

Experiment 2 had two goals. The first was to extend the results of Experiment 1 to a larger sample of glaucomatous and control subjects. The second was to test a group of ocular hypertensive patients. These patients run a risk of developing glaucoma and it was hoped that the two-pulse test might detect signs of early damage.

Extensive testing of each observer in Experiment 1 permitted a thorough representation of the psychometric functions relating level of performance to interpulse interval. While it is acceptable in the context of research to use tests extending over a period of 20 days, such tests have little practical value in a clinical setting. In medical applications the information provided by a test must be weighed against considerations such as cost and convenience. With this in mind, the procedures of Experiment 1 were scaled down. Rather than producing psychometric functions, the new procedures merely estimated thresholds for detection of a double flash. That is, they estimated the interpulse interval required to attain a criterion level of

correct responses. Furthermore, testing was restricted to an eccentricity of 3 degrees.

Position-free and position-bound tasks did not discriminate between clinical and control subjects in Experiment 1. Nevertheless, the difference in performance between the two tasks is interesting in itself. In order to confirm this effect both tasks were retained in Experiment 2.

Method

Subjects. 16 control observers and 40 patients served in the experiment. Of the 32 control eyes, 31 were normal. One eye had suffered an arterial occlusion and was blind. Control observers had no history of neurological disorders, had normal perimetric fields and were screened for any opthalmological disorders.

Of the 80 clinical eyes, 2 were normal; 39 had a history of ocular hypertension with normal perimetric fields and normal nerve heads; 39 were glaucomatous, having both ocular hypertension and perimetric field defects. Of the 39 glaucomatous eyes, 12 were unable to see at least one of the elements in the display and could not be tested. In summary, 33 normal, 39 hypertensive and 27 glaucomatous eyes were tested. To reduce experimenter bias, information regarding the diagnostic classification of a given subject was revealed only after data collection was completed.

Mean age of each group of eyes was 58 years. Median ages were 58, 58 and 62 for normal, hypertensive and glaucomatous eyes. Pupillometry equipment became available during the

course of the experiment and pupil diameter was measured in 28 normal, 31 hypertensive and 26 glaucomatous eyes. Mean pupil diameters of the three groups were: 4.1 mm, 4.4 mm and 2.8 mm for normal, ocular hypertensive and glaucomatous eyes. The 1.3 mm difference in diameter between glaucomatous and normal pupils was statistically significant (Mann-Whitney $U = 90$, $n1=15$, $n2=20$, $p<.05$). All eyes that were tested had unaided visual acuity or corrected visual acuity of no less than 6/9. It is known that visual acuity as poor as 6/60 has no significant effect on double flash resolution (Galvin et al., 1976).

Display and Procedures. Display characteristics were identical to those in Experiment 1 with the exception that the eccentricity of the outer elements was held constant at 3 degrees. Thresholds for perception of a double flash were estimated using PEST, a computerized parameter estimation procedure developed by Taylor and Creelman (1968). The procedure tracked observers' responses at all five locations in the display simultaneouly. It automatically adjusted the duration of the interpulse interval in order to converge on a point where observers responded correctly approximately 50% of the time, adjusted for chance.

All observers were tested on both position-free and position-bound tasks. Only those eyes were tested in which all five elements in the display were visible. For each observer, one threshold estimate was obtained at each location on each task for each eye. The order of testing was randomized. However, in order to reduce the amount of confusion both eyes were tested on one task before proceeding to the second task. Before each task, observers were familiarized with the procedures and were shown displays with relatively long interpulse intervals. During the course of familiarization the duration of the interval was progressively shortened until the observer started making errors. The shortest interpulse interval at which performance was error-free was used as the initial value in the PEST procedure. An entire testing sequence involving both eyes lasted about 1 - 1 1/2 hours.

Results

Results of Experiment 2 are presented graphically in Figures 14 through 23. Figure 14 shows distributions of two-pulse resolution thresholds for normal and glaucomatous eyes. The histograms include all data collected for normal and glaucomatous eyes on both tasks (position-free and position-bound) and from all five testing locations. Figure 15 shows similar distributions for normal and hypertensive eyes. A statistical treatment of the data is described below where each task is considered separately.

Results for each task are presented in Figures 16 through 19. Figures 16 and 17 show distributions for normal and galucomatous eyes. Figures 18 and 19 show distributions for normal and hypertensive eyes. The data were analyzed statistically using the Mann-Whitney U Test (Siegel, 1956). This test stipulates that all observations must be independent. That is, each observer can contribute only one score to the analysis. Consequently, the statistical analysis was performed on a subset of the data. In order to comply with the requirements of the statistical analysis, observers were divided into 3 groups: normal,

Figure 14. Histograms showing the relative frequency of two-pulse resolution thresholds for normal and glaucomatous eyes. Each eye contributed ten thresholds: five from the position-bound task and five from the position-free task.

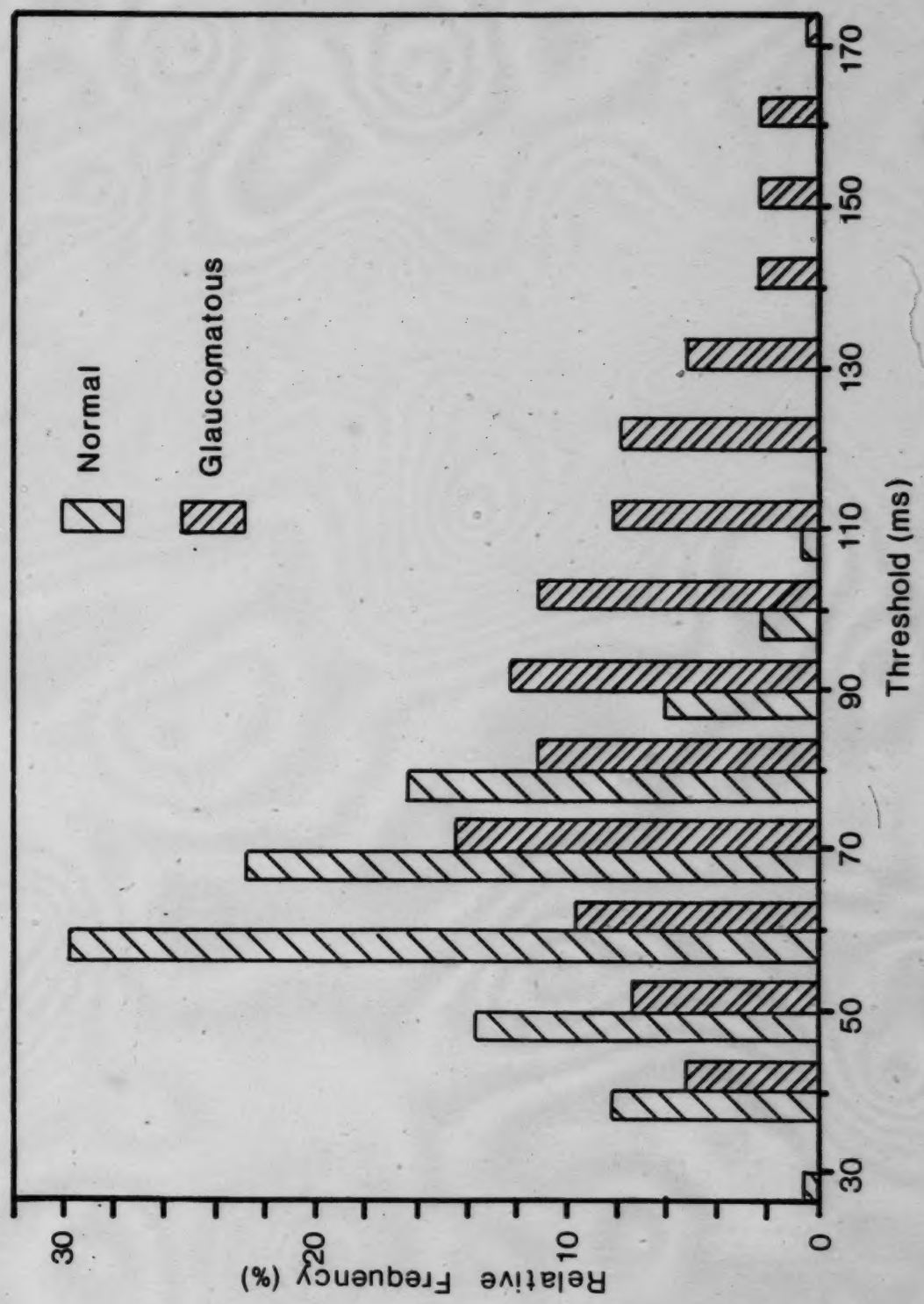

Normal
Glaucomatous
Relative Frequency (%)
0
10
20
30
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 15. Histograms showing the relative frequency of two-pulse resolution thresholds for normal and hypertensive eyes. Each eye contributed ten thresholds: five from the position-bound task and five from the position-free task.

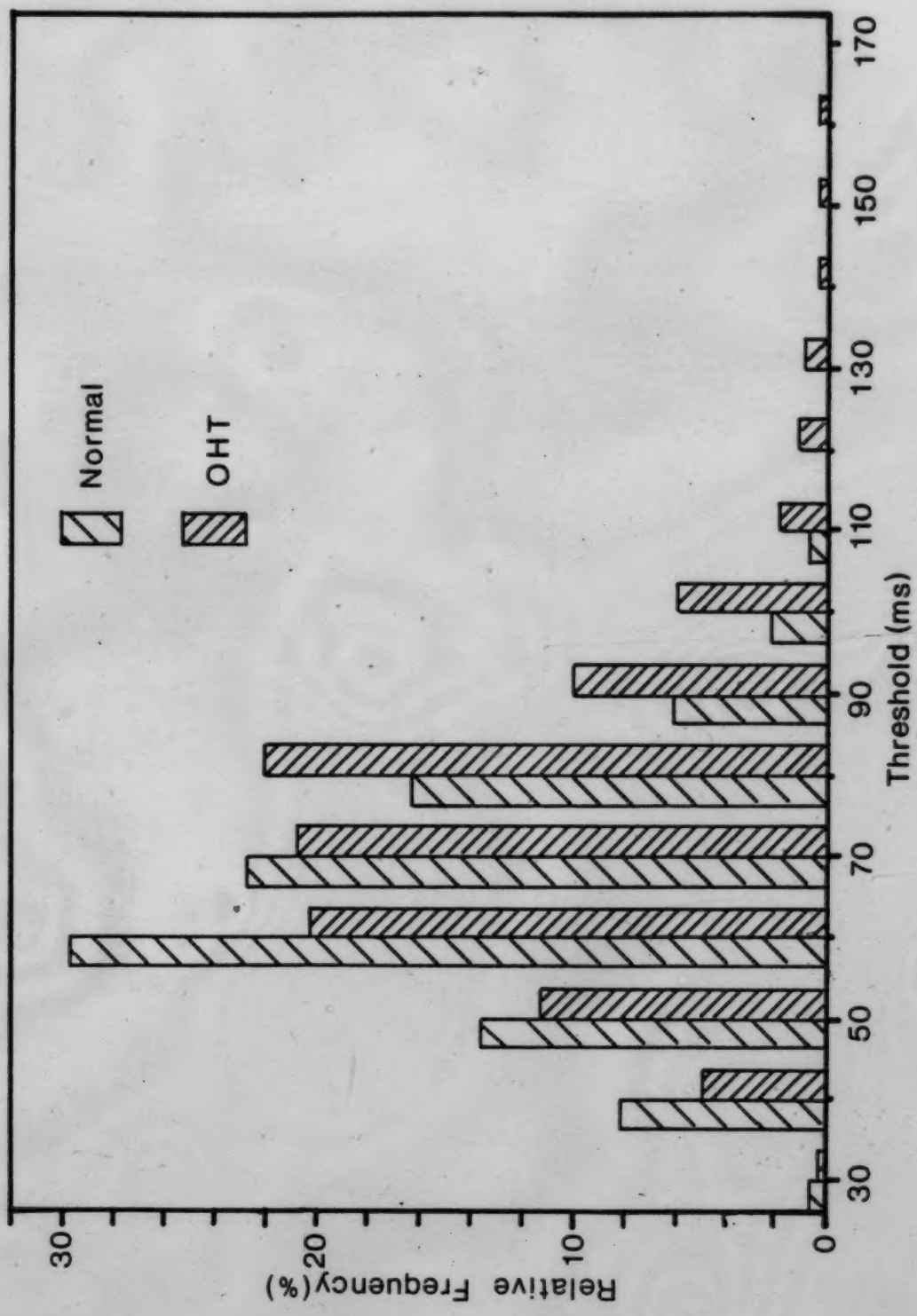

Normal
OHT
Relative Frequency(%)
0
10
20
30
Threshold (ms)
30
50
70
90
110
130
150
170

Figure 16. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-bound task for normal and glaucomatous eyes. Each eye contributed five thresholds: one from each location in the display.

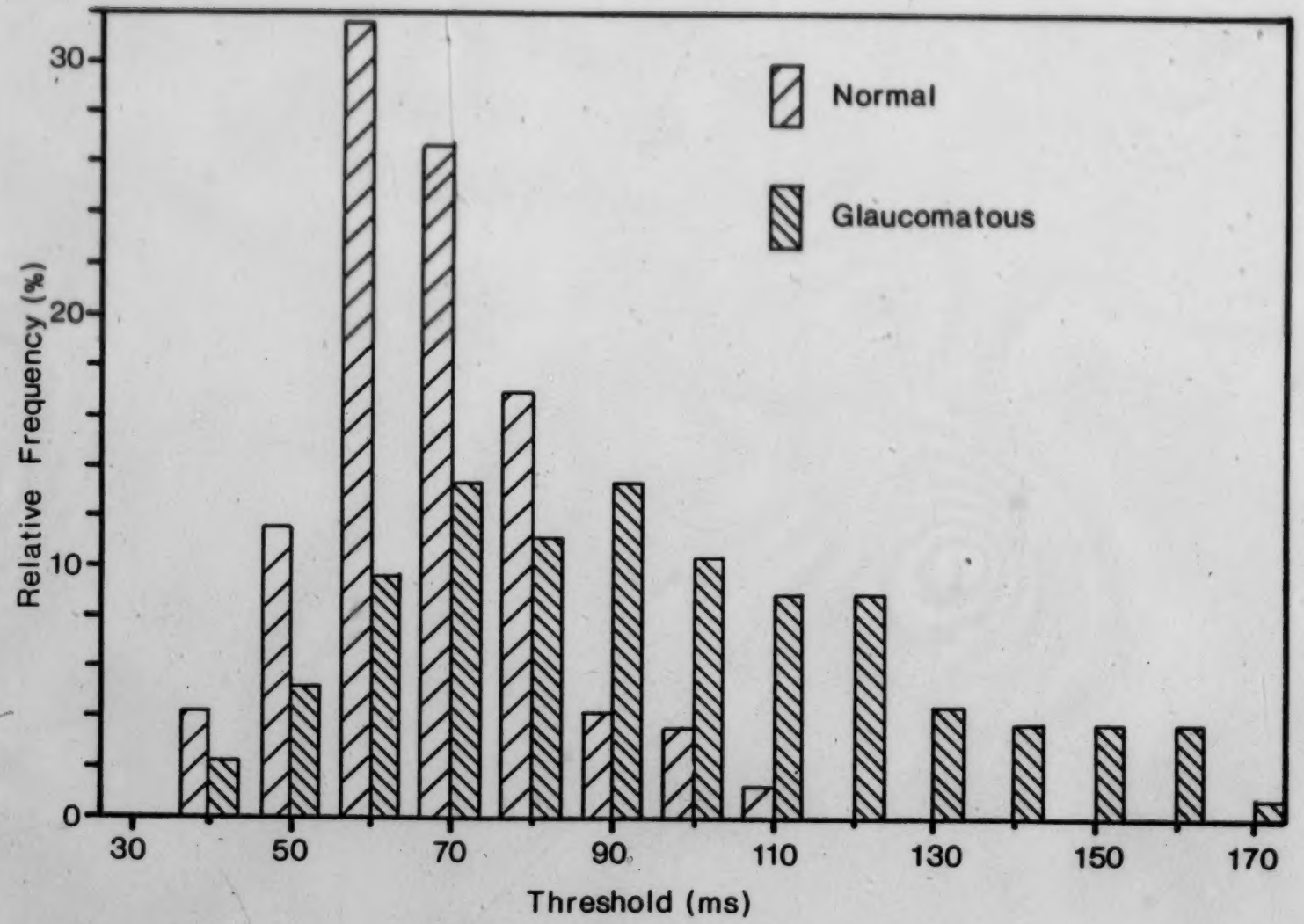

Normal
Glaucomatous
Relative Frequency (%)
0
10
20
30
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 17. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-free task for normal and glaucomatous eyes. Each eye contributed five thresholds: one from each location in the display.

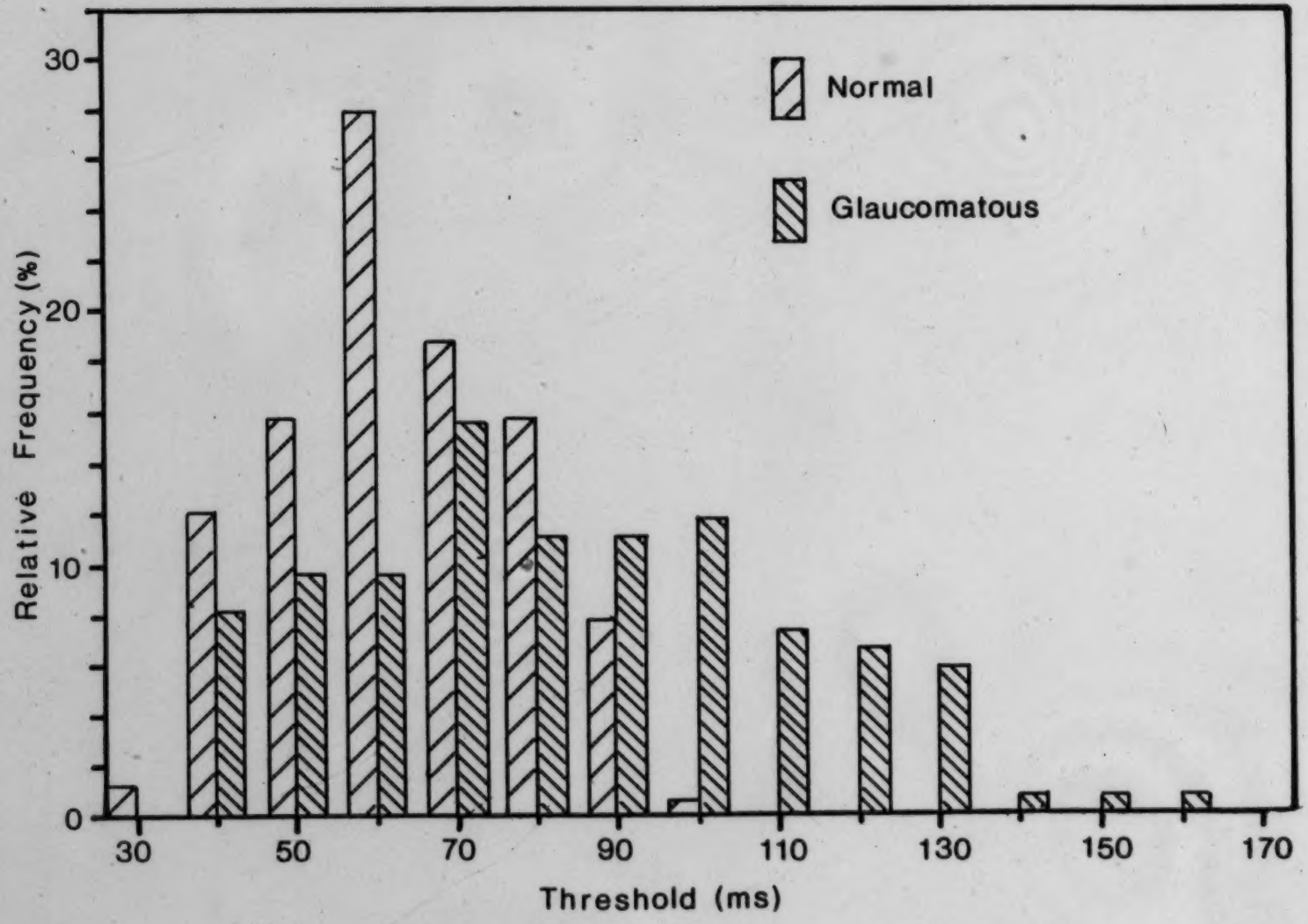

Normal
Glaucomatous
Relative Frequency (%)
30
20
10
0
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 18. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-bound task for normal and hypertensive eyes. Each eye contributed five thresholds: one from each location in the display.

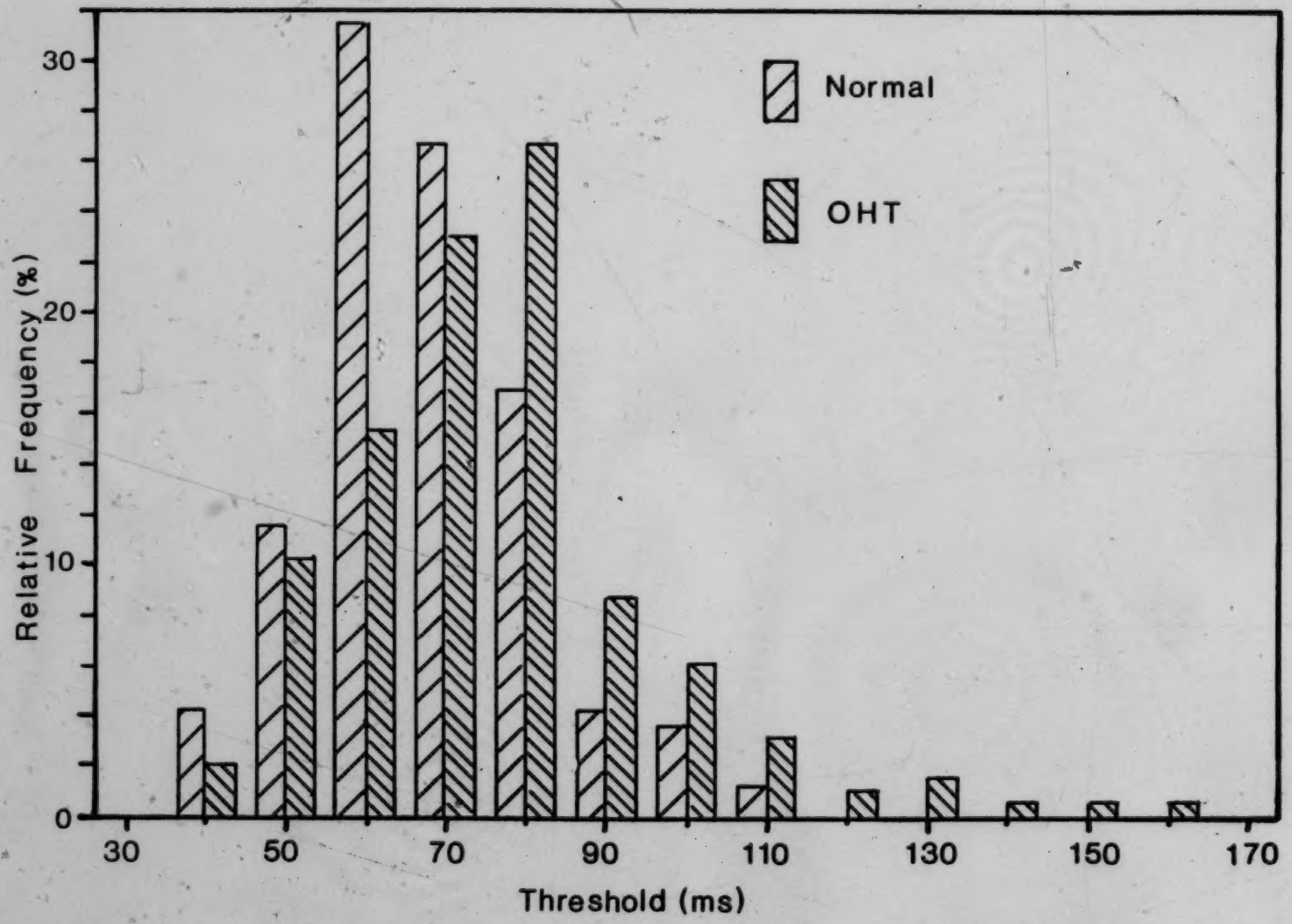

Normal
OHT
Relative Frequency (%)
0
10
20
30
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 19. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-free task for normal and hypertensive eyes. Each eye contributed five thresholds: one from each location in the display.

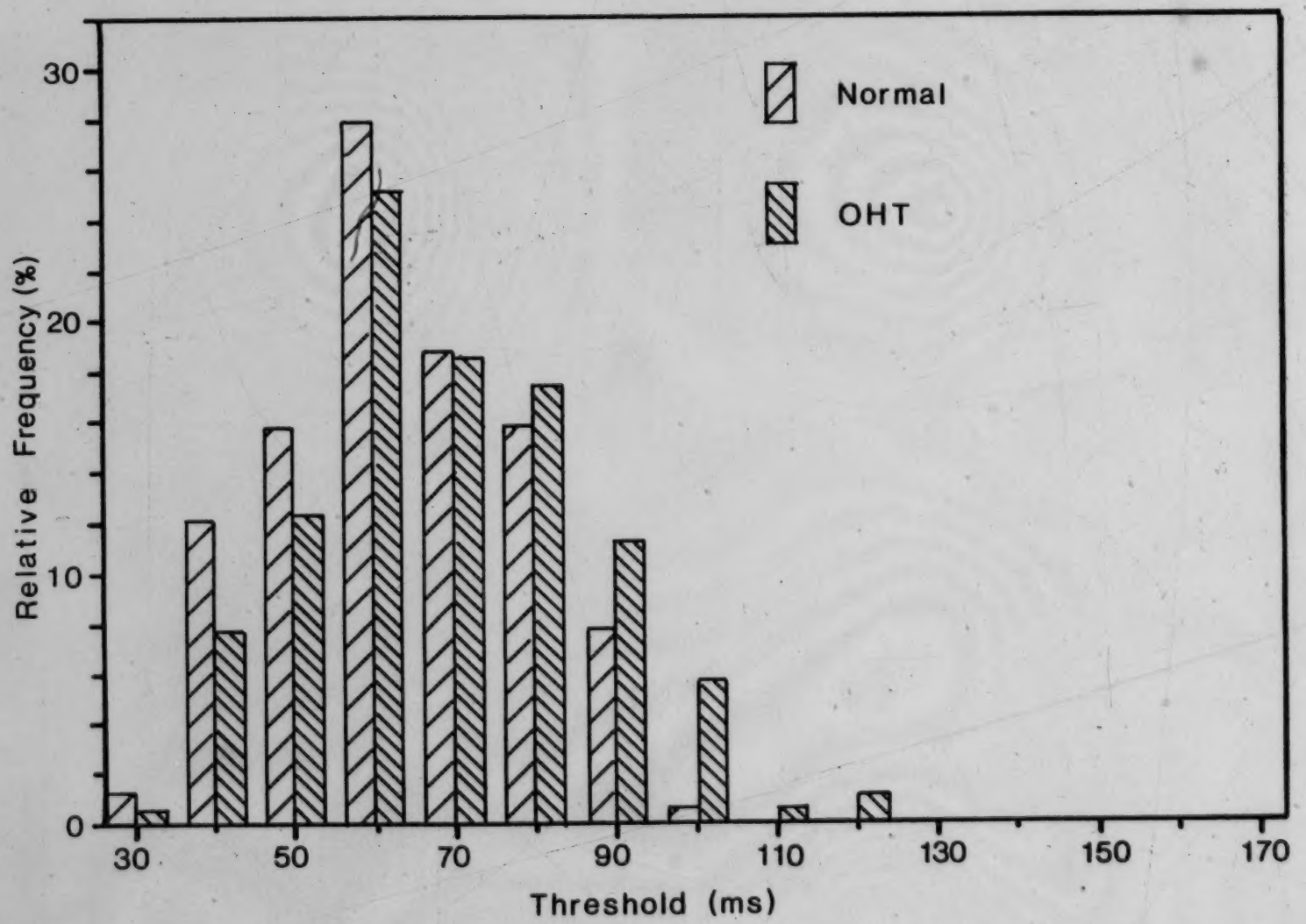

Normal
OHT
Relative Frequency (%)
30
20
10
0
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 20. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-free and in the position-bound tasks. Thresholds for normal, hypertensive and glaucomatous eyes have been combined.

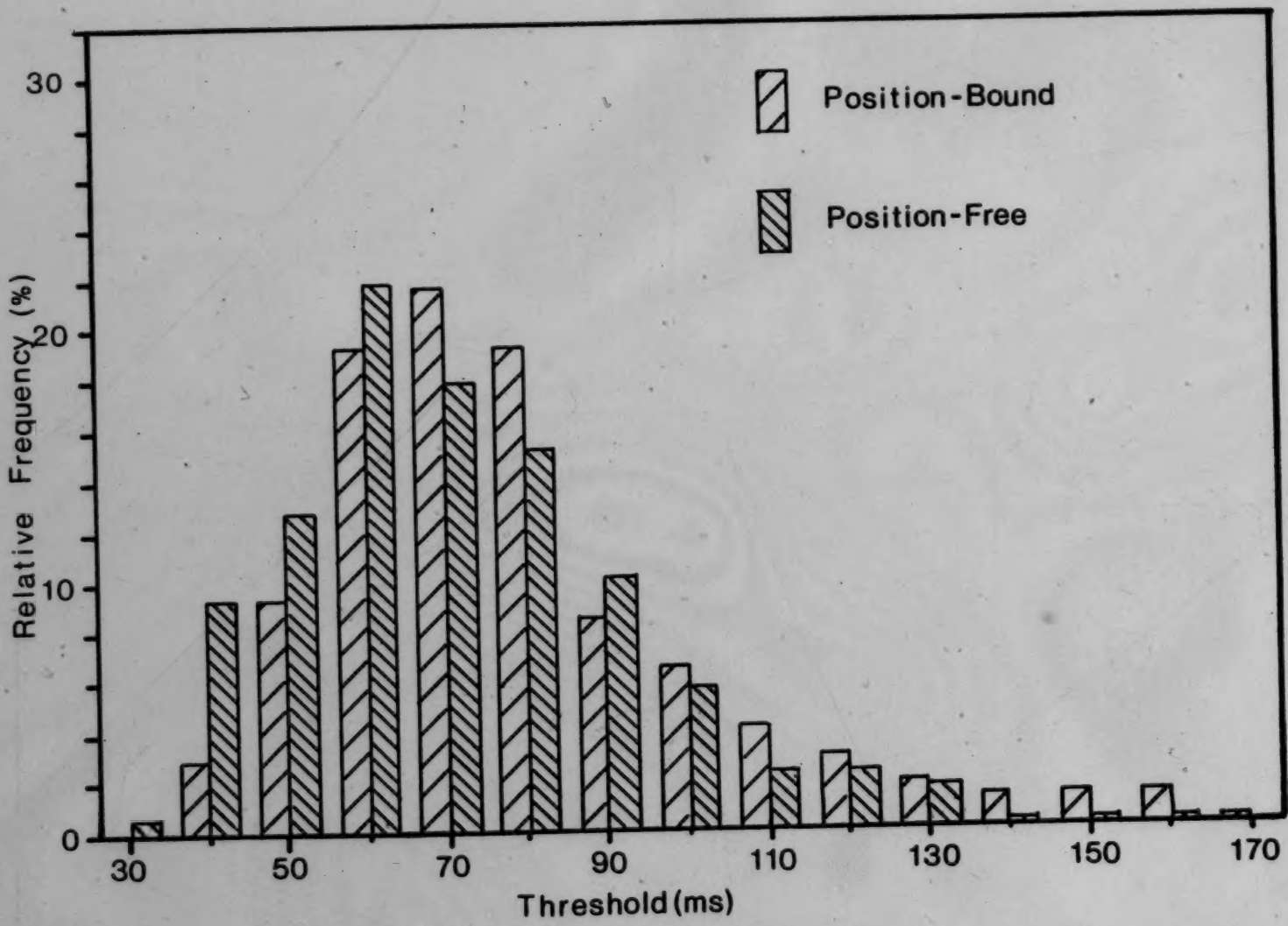

Position-Bound
Position-Free
Relative Frequency (%)
30
20
10
0
30
50
70
90
110
130
150
170
Threshold (ms)

Figure 21. Histograms showing the average two-pulse thresholds in the position-bound task at each position in the display, separately for normal, ocular hypertensive and glaucomatous samples.

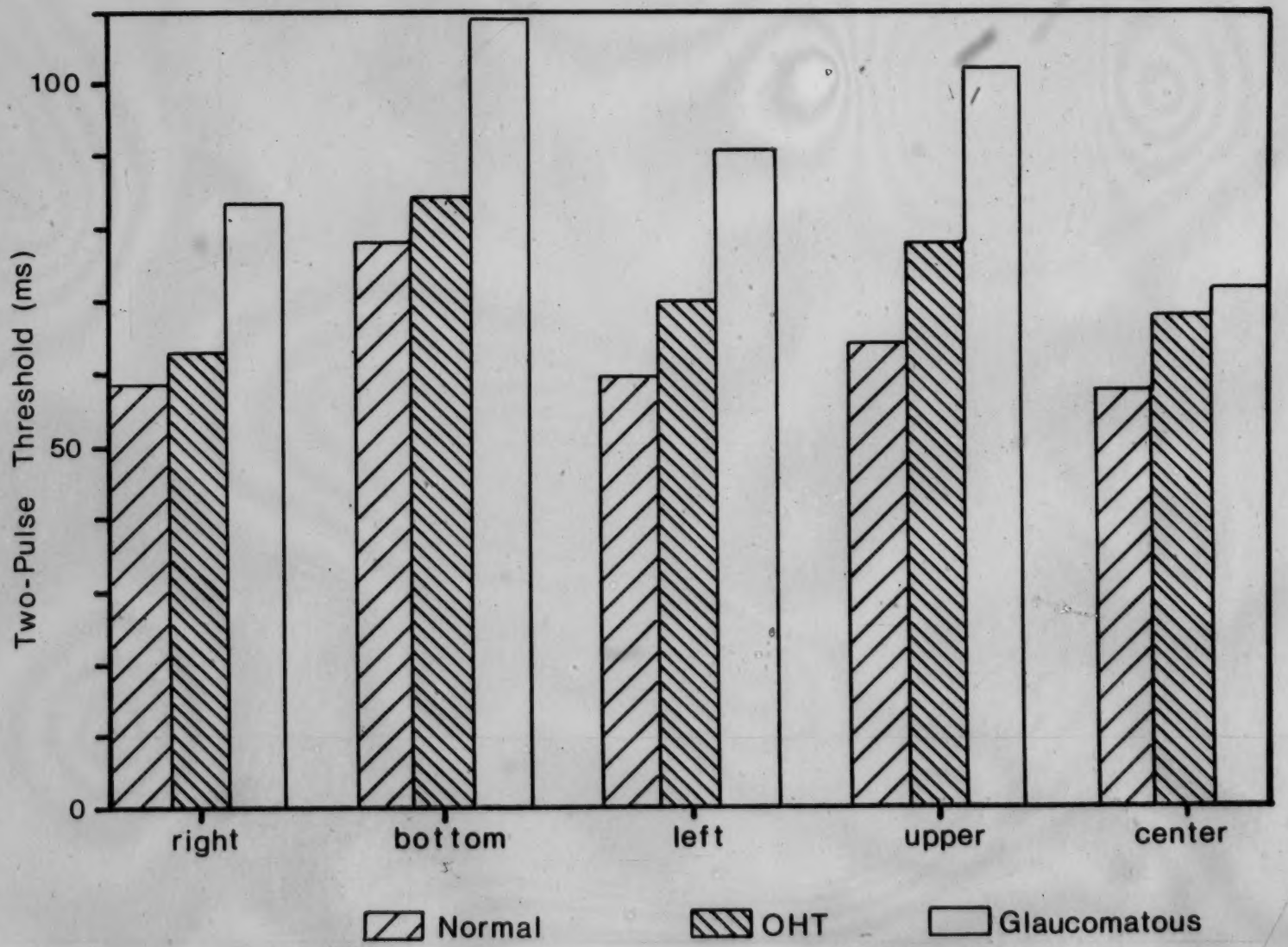

100
50
0
Two-Pulse Threshold (ms)
right
bottom
left
upper
center
Normal
OHT
Glaucomatous

Figure 22. Percentage of eyes that were judged abnormal on the position-bound task, separately for normal, ocular hypertensive and glaucomatous samples.

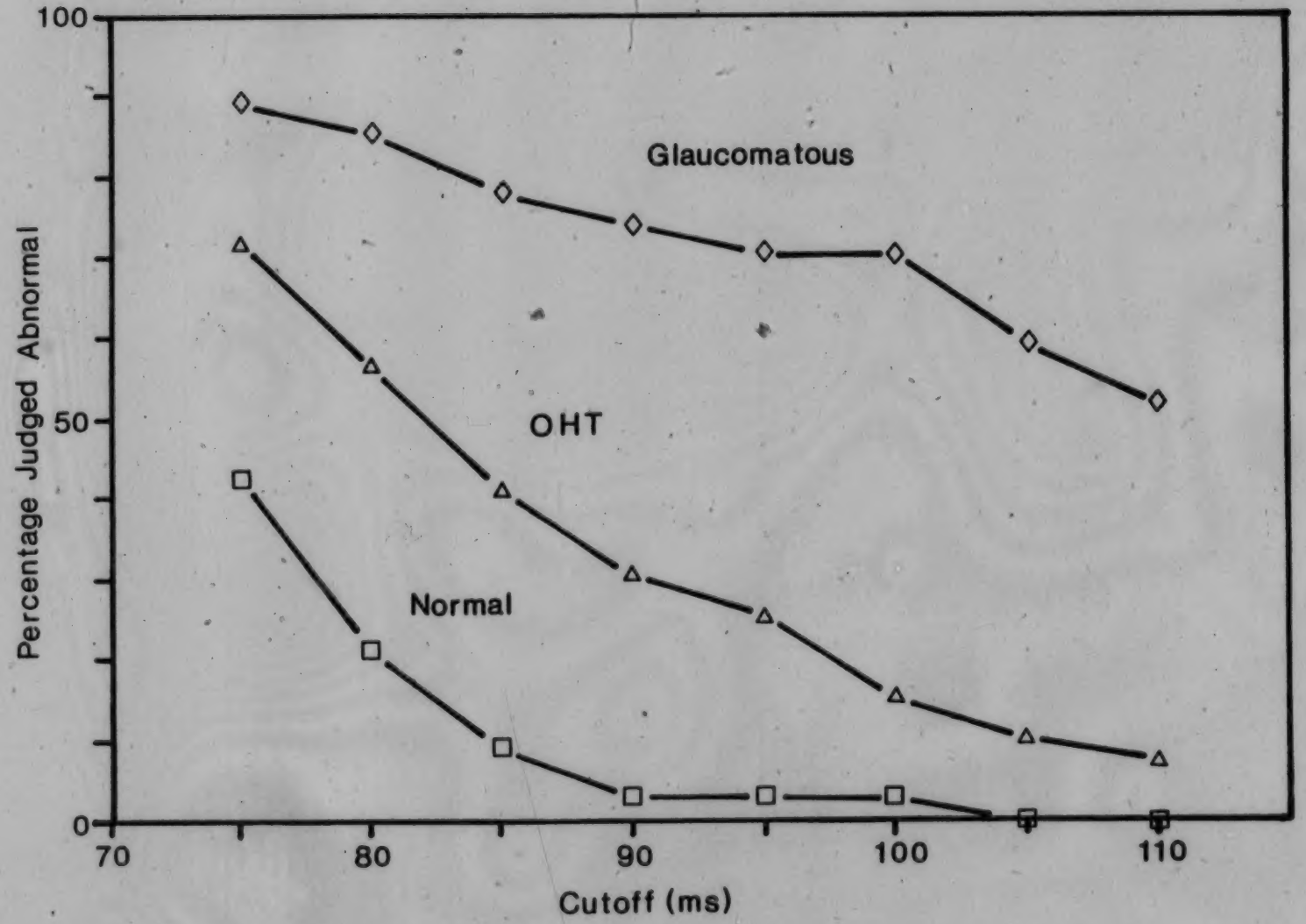
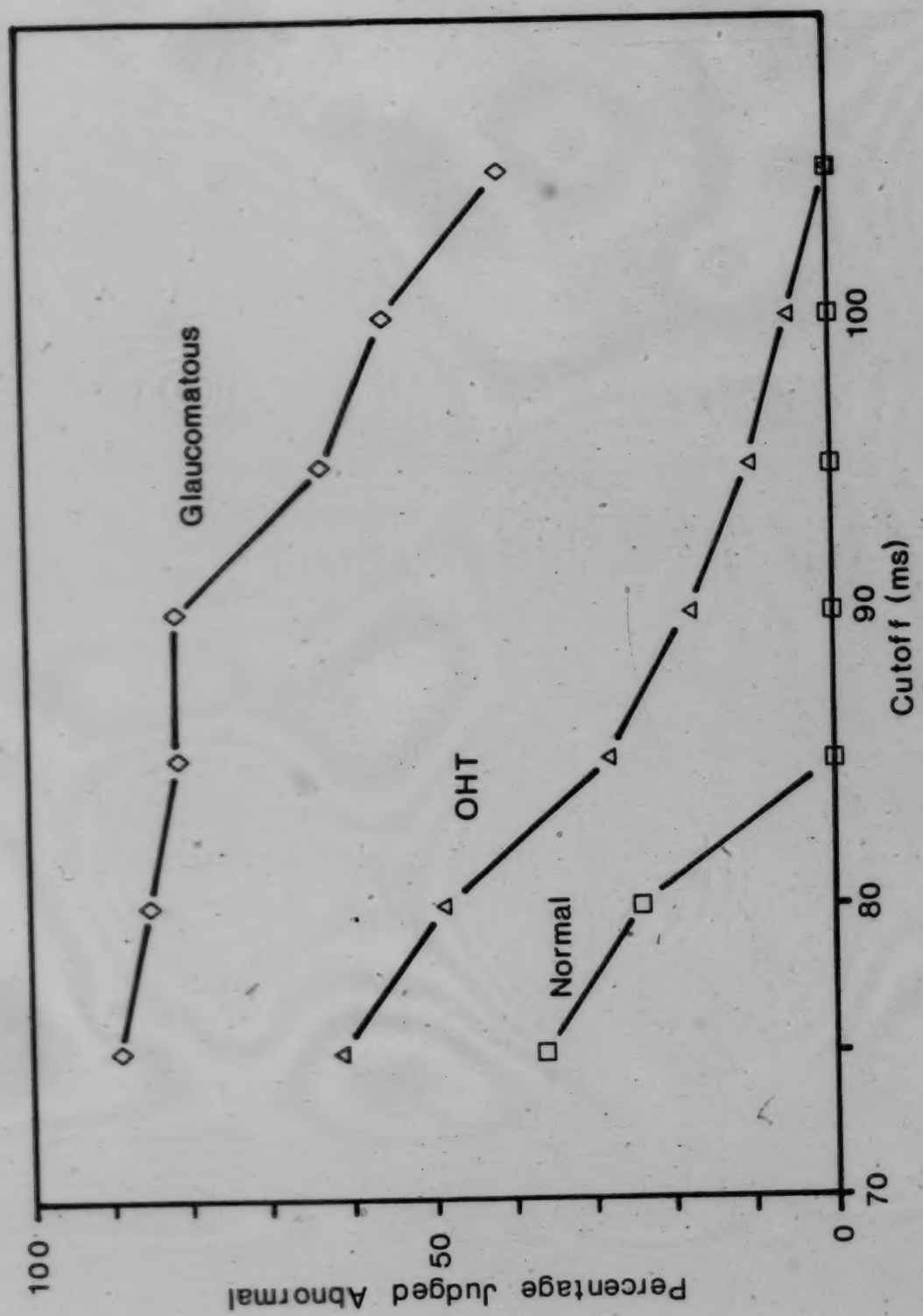

100
50
0
Percentage Judged Abnormal
Glaucomatous
OHT
Normal
70
80
90
100
110
Cutoff (ms)

Figure 23. Percentage of eyes that were judged abnormal on the position-free task, separately for normal, ocular hypertensive and glaucomatous samples.


Glaucomatous
OHT
Normal
Percentage Judged Abnormal
100
50
0
70
80
90
100
Cutoff (ms)

ocular-hypertensive (OHT), and glaucomatous, according to the following criteria: in the normal group neither eye was hypertensive or glaucomatous; in the hypertensive group both eyes were hypertensive or one eye was hypertensive and the other had not been tested because of a scotoma within 3 degrees of fixation; in the glaucomatous group at least one eye had visual field defects, but there were no scotomata within 3 degrees of fixation. Some eyes were excluded from the analysis: normal eyes of observers in the OHT group and normal or hypertensive eyes of observers in the glaucomatous group. There were 16, 19 and 21 observers in the normal, OHT and glaucomatous groups, respectively. This initial segregation of observers into separate groups facilitated extraction of independent data points. In the next step of the analysis the data were reduced from five observations per eye to a single value per observer. Since there was no a priori rationale for choosing a data-reduction method, and it was not obvious which method would provide the best separation between normal and clinical eyes, five different algorithms were investigated. In each case the five data-points from every eye were filtered according to the specified algorithm yeilding, generally, two scores per observer, one for each eye. The worst score of each observer was entered into the analysis. The five data-reduction

methods were: average all five data-points, average the two worst scores, average the two best scores, select the worst score, or select the best score.

Results of the analysis are presented in Table 1. Mann-Whitney U-scores are approximately normally distributed when there are more than 9 observers per group (Parsons, 1978), consequently the U-scores were transformed into Z-scores of the normal distribution. The significance level is shown below each score in Table 1.

It is possible to interpret the Z-scores in Table 1 as indices of separation between groups achieved by a given data-reduction method. This is so because the Mann-Whitney test ranks all data points prior to computing the U statistic. Consequently, the U statistic reflects the degree to which two distributions overlap. In Table 1 large numerical values of Z are associated with distributions that have little overlap. For each comparison the largest and next largest Z-scores have been underlined. The best overall separation between control and clinical distributions was obtained by averaging the two worst thresholds. Using this method of data-reduction all comparisons were significant at least at the .05 level. Given the large number of

Table 1. Z-scores and probability levels for comparisons listed in the left column for each type of data-reduction algorithm listed along the top. The largest and next largest scores for each comparison have been underlined.

	average of two worst	worst	average of two best	best	average all
Posit.-bound Normal-Glauc.	3.89 P<.0002	3.65 P<.0003	3.28 P<.001	1.9 N.S.	3.92 P<.0001
Posit.-free Normal-Glauc.	4.2 P<.0001	4.08 P<.0001	2.21 P<.03	1.47 N.S.	3.68 P<.0003
Posit.-bound Normal-OHT	2.19 P<.03	1.39 N.S.	1.99 P<.05	0.86 N.S.	2.28 P<.02
Posit.-free Normal-OHT	2.15 P<.03	1.82 N.S.	1.52 N.S.	1.19 N.S.	1.95 N.S.
Posit.-bound Glauc.-OHT	2.88 P<.04	2.91 P<.004	1.91 N.S.	1.34 N.S.	2.72 P<.007
Posit.-free Glauc.-OHT	3.59 P<.0005	3.62 P<.0003	1.1 N.S.	0.34 N.S.	3.02 P<.003

comparisons, one may wish to regard some of the Z-scores as being only marginally significant.

Figure 20 shows the data separately for the two tasks collapsed over all groups. The data were analyzed with a Friedman Two-way Analysis of Variance for within-subject factors (Siegel, 1956). The difference between tasks was significant at the .01 level (chi squared was 9 with 1 d.f.).

Figure 21 shows average two-pulse resolution thresholds at each location in the display for the position-bound task. The position-free task yielded a similar pattern.

Sensitivity of the present method and its potential value in a clinical setting can be assessed from Figures 22 and 23. These figures show the percentage of eyes that were judged abnormal in each group at different criterion values for abnormality. The criteria, shown along the X-axis, can be thought of as boundaries between normality and abnormality. They were applied to the average of the two worst scores which, as mentioned above, provided the best overall separation between groups. Two-pulse thresholds equal to or greater than the boundary value were deemed to be abnormal. The optimal cutoff between normality and

abnormality was in the range between 85 and 95 ms. Within this range, few eyes from the control group were judged abnormal, whereas a substantial proportion of clinical eyes were abnormal.

Two-pulse resolution thresholds were correlated significantly with age for control eyes ($r = 0.43$, $t = 2.61$, $d.f. = 31$, $p<.01$), but not for hypertensive or glaucomatous eyes. Thresholds were not correlated with pupil-size for any group.

The significant correlation with age in the control sample replicates results reported by Pearson and Tong (1968). Absence of a correlation in the clinical samples cannot be ascribed to differences in the range of the independent variable. In fact, the range of ages was greater in the clinical samples (the ranges were: 41-68, 27-73 and 38-71 for control, ocular hypertensive and glaucomatous samples, respectively). Rather, lack of correlation in the clinical samples is due to the greater variability amongst the threshold scores for pātients at any given age.

Discussion

The goal of Experiment 2 was to examine how well the two-pulse resolution method could separate between control and glaucomatous eyes as well as to evaluate its potential use for detecting early damage associated with elevated intaocular pressure. Judging from the distributions of scores shown in Figures 14 through 19 it can be said that a fair degree of separation was achieved between the three groups: control, ocular hypertensive and glaucomatous. Overall, glaucomatous eyes required the longest interpulse intervals to attain criterion-level performance on the two-pulse resolution task, followed by hypertensive eyes and control eyes. Both shape and central tendency distinguished the distributions of clinical and normal samples. The greater variance of the clinical distribution is due, in part, to the variability of thresholds at different retinal locations (Figure 21) and, in part, to the varibility between observers.

All groups had shorter thresholds in the position-free task than in the position bound-task, but again the tasks did not differ in their capacity to separate clinical from

control populations. Compare the displacement of the lightly shaded bars relative to the thickly shaded bars in Figures 16 and 17, or in Figures 18 and 19. The slightly greater displacement in the position-bound task which is evident in the graphical comparison was not confirmed by the statistical analyses. Note that the Z scores in Table 1 show no consistent advantage of one task over the other.

Hypertensive eyes. An important aspect of Experiment 2 concerns the results from the group of hypertensive eyes (Figures 15, 18 and 19). It should be stressed that these eyes had normal perimetric fields and normal optic nerve heads. Their only clinical symptom was an elevated intraocular pressure. Nonetheless, their thresholds for perceiving a double pulse were lengthened, suggesting that visual damage was already present.

It may seem paradoxical that the same retinal location is able to detect a single flash of light normally, yet be impaired at detecting a gap between two flashes which follow each other in rapid succession. The paradox rests on the assumption that the same factors are responsible for detection of both events: single pulses and gaps between pulses. Actually, the underlying factors are different. In

the first case, accuracy of detection depends on the amplitude of the response produced in the visual system. Provided the amplitude exceeds some minimal value, a single flash can be percieved. However, in the latter case, both flashes must not only be visible, but also be separable in time. Here, response amplitude does not adequately characterize the behaviour of the visual system (Boynton, 1972). The additional factor needed to explain the effects of a two-pulse stimulus is the rate of recovery from stimulation. If the second pulse is displayed before the system has had time to recover, it is likely that the percept will not reflect accurately the time-course of the stimulus. Under these circumstances, both pulses may blend together and an observer will be more likely to perceive one flash rather than two. On this view, impairement in two-pulse resolution observed in hypertensive eyes may be caused by a relatively slow rate of recovery from stimulation. More generally, the impairment may arise from an attenuation of the high temporal frequencies of the two-pulse target. Since these frequencies produce the sharp onsets and offsets of each pulse, the effect of this attenuation would be to transform the two square pulses of the target into two gently undulating waves, as well as to delay the peaks of the waves (see Figure 1). Phenomenologically, this could produce a sensation of

"temporal smudging" or elongation of the percept of each pulse, resulting in poor resolution of the two-pulses.

Impairement in two-pulse resolution observed in glaucomatous eyes can be explained in a similar manner. However, in glaucomatous eyes it is possible that both recovery rate and response amplitude were abnormal. This is suggested by phenomenological reports of four observers who noted that some of the elements in the display appeared dimmer than the others. Dimmer elements also had longer two-pulse thresholds. Nevertheless, it is unlikely that impaired brightness perception is a prerequisite for two-pulse resolution deficits in glaucoma. A direct examination of this possibility is described below in Experiment 3 where it is shown that brightness perception of glaucomatous eyes is unrelated to abnormalities in temporal resolution.

In follow-up investigations of the current sample of patients it would be interesting to examine brightness perception of retinal locations which showed temporal deficits in the present work. If the double pulse technique is able to detect retinal locations which have a high probability of developing perimetric field defects, the

technique could be used in a clinical setting to identify those patients which need intensive therapy. Ideally, the technique might identify visual damage at a stage where it is still reversible.

Physiological correlates. Little is know about physiological correlates of psychophysical abnormalities in glaucoma, especially in the early stages of the disease. For this reason it would be premature to suggest a physiological account of the deficits observed here. What might be said with some degree of certainty is that glaucoma and OHT do not share the physiological basis for the two-pulse deficit with similar deficits in multiple sclerosis. Axonal demyelination which is a suspected cause in multiple sclerosis, is not a prominent factor in glaucoma or OHT (Galvin et al., 1976). In the latter, metabolic disturbances in rod and cone function or blockage of axonal transport might play a role (Quigley, 1983).

At a coarser level of analysis, there is some concordance between the present results and those reported from photographic studies of deterioration of the nerve fiber layer in OHT and glaucoma. Airaksinen et al. (1984) reported that a generalized loss of nerve fibers was more common in

eyes with glaucoma than in eyes with hypertension. Our results show that two-pulse resolution deficits were both more common (see below) and more severe in glaucomatous patients. It may be that severity of impairment in two-pulse resolution is correlated with the amount of diffuse damage to the nerve fiber layer. Of course "diffuse damage" does not imply "uniform damage" as evidenced by the variability in degree of impairment of glaucomatous eyes at different locations in the display (Figure 21). It would be interesting to correlate point by point the distribution of damage to the nerve fiber layer with the severity of impairment in two-pulse resolution.

Attentional factors. While an impaired two-pulse threshold at a given location may reflect early retinal damage, it is possible that attentional biases may have lead to an overestimate of the severity of damage. That is, patients may have become aware of their impairment at a given retinal site and may have ignored, at least to some degree, stimuli at that site, thus leading to prolonged estimates of two-pulse threshold. In future work this possibility might be investigated with a validating procedure that employed a display consisting of a single stimulus. Under these conditions it would be less likely that attentional biases

could affect estimates of threshold because observers would be less likely to divert their attention away from the single target.

Position-free and position-bound tasks. A reliable advantage of the position-free task over the position-bound task was found in Experiments 1 and 2. As mentioned earlier, the display characteristics of the two task were identical, but the response procedures differed. In the position-bound task observers were required to identify the location of the target, whereas in the position-free task they were required only to identify the display interval in which the double-pulse occurred.

Wilson and Singer (1981) report an effect which may shed some light on the difference between the two tasks. In their experiment, two stimuli were presented, separated by up to 25 degrees of visual angle. One stimulus was designated as the target, and the other was designated as the mask. In the conditions of interest, the target was a single 30 ms pulse, and the mask was a double pulse, or vice versa. On about 1/3 to 1/2 of the trials, observers reported that the target acquired the appearance of the mask. That is, a single-pulse target looked like a double-pulse and a double-pulse looked

like a single-pulse. Similar interactions might have influenced estimates of the two-pulse resolution threshold here. On the one hand, the effect of the single-pulse distractors would have been to diminish the likelihood of perceiving the two-flash target. In this instance, both position-free and position-bound tasks would have become more difficult, resulting in longer estimates of two-pulse resolution thresholds. On the other hand, the effect of the two-pulse target would have been to induce the appearance of double flash in the single pulse distractors. This would have impaired one's ability to name the location of the true target, but not to identify the interval in which it occurred. A pattern of interactions like this might explain the relative superiority of the position-free task. Parenthetically, Wilson and Singer ascribe the interaction of single-pulse and double-pulse stimuli to relatively central processing centres in the visual system.

Diagnostic yield. The level at which a two-pulse threshold might be judged significantly abnormal can be taken as 2.3 sample standard deviations above the mean of the distribution for normal eyes. By this criterion about 1% of normal eyes would show a spurious abnormality. This level corresponds to 94.5 ms and 92.3 ms for position-bound and

position-free tasks, respectively. Based on these limits, about 26% of OHT eyes were abnormal on the position-bound task and about 15% were abnormal on the position-free task. The corresponding figures for glaucomatous eyes were 70% and 63%. See Figure 22 and 23 for a detailed breakdown.

At first glance, diagnostic yield of the present technique does not compare favourably with the temporal visuogram which classified about 90% of hypertensive eyes and 100% of glaucomatous eyes as abnormal (Tyler, 1981). There are at least three reasons for this discrepancy.

As the duration of ISI of a two-pulse target is shortened, its power spectrum shifts toward higher temporal frequencies. As a result, the visual system's sensitivity to high temporal frequencies may set the threshold duration of the ISI at which a double flash is visible. Unfortunately, the temporal frequencies at the extreme end of the visible range may not be the site of maximal impairment in temporal functioning. In fact, in Tyler's study 20-25% of hypertensive and glaucomatous eyes showing significant impairment at intermediate temporal frequencies (20-30hz) would have been diagnosed as normal at the highest visible frequency.

Testing parafoveal as well as foveal locations may also have contributed to the greater sensitivity of Tyler's method. It is known that in glaucoma the parafovea is more susceptible to damage than the fovea. Indeed, if we examine only the foveal test site the sensitivity of Tyler's method drops to about 75% for hypertensive eyes and to about 83% for glaucomatous eyes.

Temporal frequency range and placement of stimuli accounts for about 35% - 45% of the discrepancy between the sensitivity of the two methods. This is adequate to explain the difference between glaucomatous samples, but not between ocular hypertensive samples. The greater magnitude of the discrepancy in the latter group may depend on differences in the composition of the samples. In Tyler's study 75% of hypertensive eyes had fellow eyes with field defects. The comparable figure in the present work was only 21%. It is well known that a hypertensive eye with a glaucomatous fellow eye is more likely to develop perimetric field defects than a similar eye with a nonglaucomatous fellow eye (Harbin, Podos, Kolker & Becker, 1976; Susanna, Drance & Douglas, 1978). One might also expect that the likelihood of detecting early damage would be higher when the fellow eye is glaucomatous.

In part, this may explain the greater diagnostic yield in Tyler's sample of hypertensive eyes. It would be interesting to examine this possibility directly by comparing the sensitivity of the visuogram in samples of hypertensive eyes with and without glaucomatous fellow eyes. In the present work there were to few hypertensive eyes with glaucomatous fellow eyes to permit meaningful comparisons.

Experiment 3

It is known that temporal effects in vision are related to the brightness of the stimulus (Onley and Boynton, 1962). Specifically, it is known that two-pulse thresholds are inversely related to brightness. That is, bright stimuli yield shorter two-pulse thresholds than dim stimuli (Kietzman, 1967; Lewis, 1967). However, this clearly does not imply that the temporal threshold elevations in the glaucomatous and hypertensive samples were artefacts resulting from diminished sensitivity to light. Nevertheless, it is important to show that the severity of impairment in two-pulse resolution at a given retinal location was not related to the perceived brightness at that location.

Perceived brightness was assessed using a matching technique. The technique provided an estimate of the luminance at which a test stimulus had to be displayed in order to appear as bright as a standard. In practice, a given retinal location could require more, less, or the same level of luminance as the standard in order to match it in terms of brightness. If a location required more luminance,

this indicated that it was less sensitive than the location of the standard. Requiring less luminance, or the same level of luminance indicated greater or equal sensitivity, respectively. A similar statement can be made regarding the two-pulse resolution thresholds at the various locations: the duration of the interpulse interval at threshold could be either longer, shorter or equal to the duration at the location of the standard. If diminished sensitivity to light were a necessary condition for deficits in temporal resolution, then we might expect that retinal locations with longer two-pulse thresholds than the standard would also require more luminance to match the brightness of the standard.

Method

Design and Procedures. With the exceptions noted below, observers, display, design and procedures were the same as in Experiment 1.

The central element was designated as the standard and the outer elements were the test stimuli. All elements were displayed in a single pulse for a duration of 100 ms. This was the shortest duration which provided a sufficiently large range of brightness values. The luminance of the central element was held constant at 3.5 cd/m^2, whereas the luminance of the surrounding elements varied. At the beginning of a session two of the surrounding elements, chosen randomly, were set 1.5 cd/m^2 below that of the central element. The remaining two were set 1.5 cd/m^2 above that of the central element. At these settings, two of the outer elements looked distinctly brighter and two looked distinctly dimmer than the central element.

On any given trial, only two elements were displayed: the central element and one outer element. The observer's task was to indicate which element appeared brighter (central or outer). PEST, a computerized parameter estimation technique (Taylor and Creelman, 1967) tracked the observer's responses and adjusted the luminance of the outer element until it was selected 50% of the time. That is, until the observer was no longer able to discriminate between the central element and the outer element in terms of brightness. It was assumed that at this level of luminance the outer element was matched in terms of brightness with the central element.

The outer elements were displayed at three eccentricities (2, 3, and 4 degrees). Within a given session, eccentricity was held constant at one level, while the location at which the outer element was displayed (top, bottom, right or left) varied randomly from trial to trial. At the end of a session, PEST reported the luminance values at which the outer elements matched the central element in terms of brightness. The luminance of the central element (3.5 cd/m^2) was subtracted from these values to reflect the amount by which the brightness at each test site differed from that at the central location. In total, there were 12 test sites defined by the combination of four positions and three eccentricities. The matching procedure was repeated three times at each test site, and the average value was used in the analysis. Each observer was tested over a period of 1 1/2 hours.

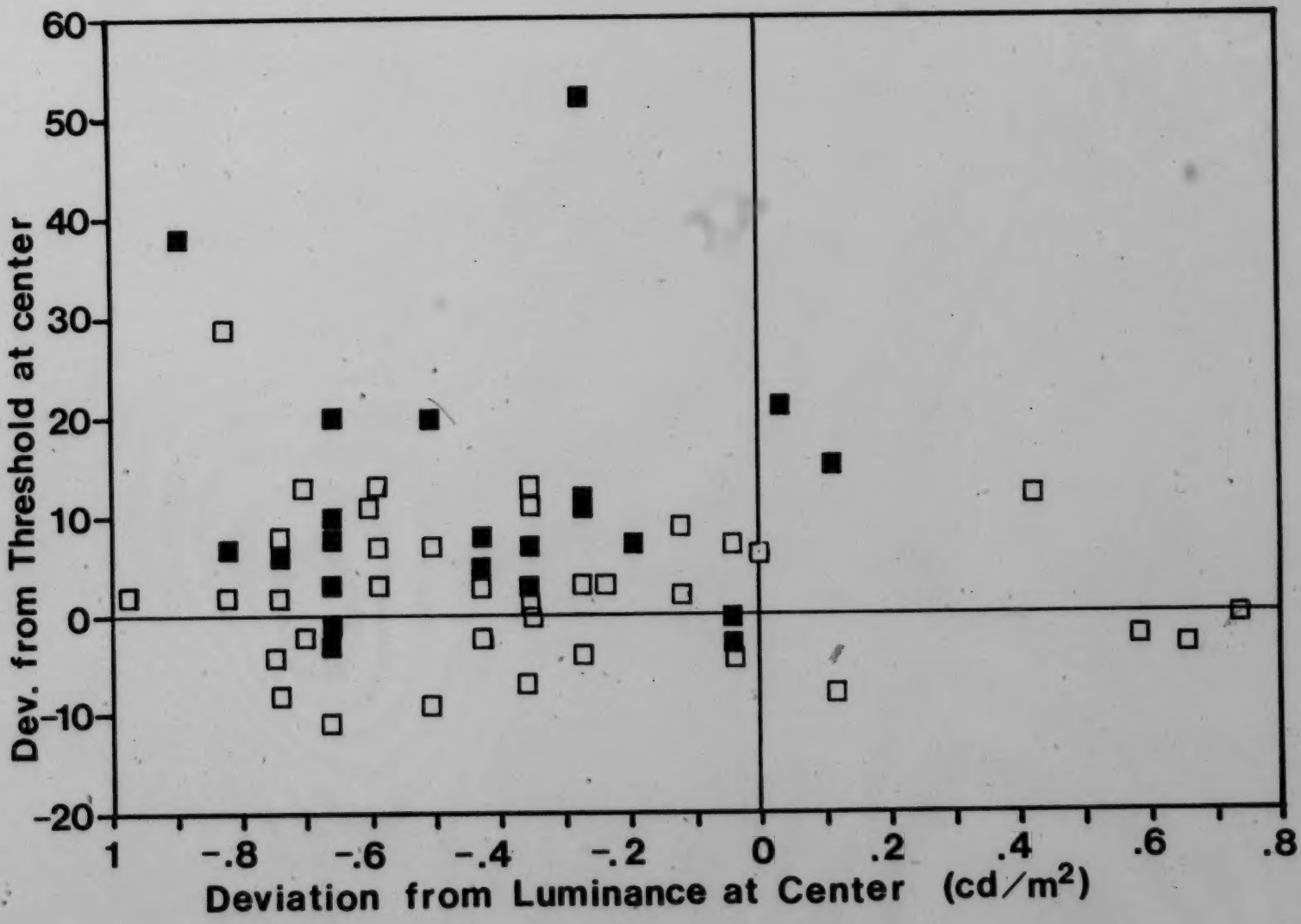
Two-pulse resolution threholds (50% correct responses above chance) were estimated from the psychometric functions obtained in the position-bound task in Experiment 1. The threshold value of the central location was subtracted from the values at each of the twelve test sites. The result reflects the amount by which the interpulse interval at each site deviated from threshold at the center.

Results

Results of Experiment 3 are shown in Figure 24. Each square represents results from one test site of one observer. Filled squares represent glaucomatous eyes, open squares represent control eyes. The position of each square along the X-axis was determined by the luminance at the particular site that was required to match the brightness of the standard. Negative values indicate that less luminance was required while positive values indicate than more was required. For example, if the matched luminance was 3.9 cd/m^2 (nits), the point in Figure 24 would be located at 0.4 nits on the X-axis which is 3.9 nits minus the standard luminance of 3.5 nits. The position of each square along the Y-axis was determined by the interpulse interval at the particular site that was required to achieve threshold on the position-bound task. Positive values indicate that a longer interpulse interval was required at the given site than at the central location. Negative values indicate the opposite.

On the hypothesis that brightness perception and two-pulse resolution thresholds are related, we would expect that a given location requiring a relatively high luminance

Figure 24. Scatter diagram showing the two-pulse threshold at a given retinal location plotted against the luminance required to match the brightness at the central location. Values have been rescaled to reflect the deviation from the value at the central location. Filled points represent glaucomatous eyes. Open points represent control eyes.


60
50
40
30
20
10
0
-10
-20
Dev. from Threshold at center
1
-.8
-.6
-.4
-.2
0
.2
.4
.6
.8
Deviation from Luminance at Center (cd/m²)

to match the brightness at the center, should also require a relatively long interpulse interval to match the two-pulse threshold at the center. No such relationship is evident in Figure 24. Overall, the duration of the interpulse interval was unrelated to the matched luminance. This suggests that the impairment observed in glaucomatous eyes in Experiment 1 cannot be ascribed to deficits in light perception.

One other aspect of the results is worthy of comment. The clustering of points in the left half of Figure 24 indicates that the outer locations appeared as bright as the central location at slightly lower levels of luminance. This suggests that the sensitivity of the central position may have been diminished relative to the outer positions. Desensitization may have resulted from an elevated adaptation level produced by neighboring fixation dots as well as from the repetitive stimulation by the "standard" element. Alternatively, parafoveal retinal areas may be inherently more sensitive to light under the mesopic light levels of the present work.

Experiment 4

Experiment 4 set out to validate the present technique for measuring two-pulse resolution thresholds by testing a sample of patients with multiple sclerosis. Galvin et al (1976, 1977) have reported that thresholds of such patients were significantly impaired.

Method

Twelve patients with clinically definite multiple sclerosis and six age-matched control subjects served in the experiment. Of the 24 clinical eyes, six had experienced an episode of retrobulbar neuritis. Of these six, three could not see all the elements in the display and were not tested. The remainig 18 clinical eyes had no history of optic neuritis. All 21 clinical eyes which were tested had visual acuity of no less than 6/9. Control observers were neurologically and ophthalmologically sound. All 12 control eyes were tested. Display and procedures were identical to those in Experiment 2.

Results

Results of Experiment 4 are shown in Figures 25, 26and 27. Overall, eyes of patients with multiple sclerosis had longer two-pulse resolution thresholds than control eyes (Figure 25). The impairment was evident on both position-free and position-bound tasks (Figure 26 and Figure 27). The differences were statistically significant at the .002 level. Mann-Whitney U scores were 60 and 63.5 (n1=6, n2=12) for position-free and position-bound tasks respectively. The analysis was based on the average of the two worst scores for both groups of eyes. Details of the statistical procedures are described in the Results section of Experiment 2.

The limit of normality was defined as 2.3 standard deviations above the control mean which corresponds to an interpulse interval of about 81 ms. Based on the average of the two worst scores, 38% (8/21) of clinical eyes fell outside this limit. All three eyes with a history of optic neuritis were classified as abnormal. Five eyes without optic neuritis also had prolonged two-pulse thresholds. This pattern of results agrees with the major aspects of the work

Figure 25. Histograms showing the relative frequency of two-pulse resolution thresholds for normal eyes and eyes of patients with multiple sclerosis. Each eye contributed ten thresholds: five from the position-bound task and five from the position-free task.

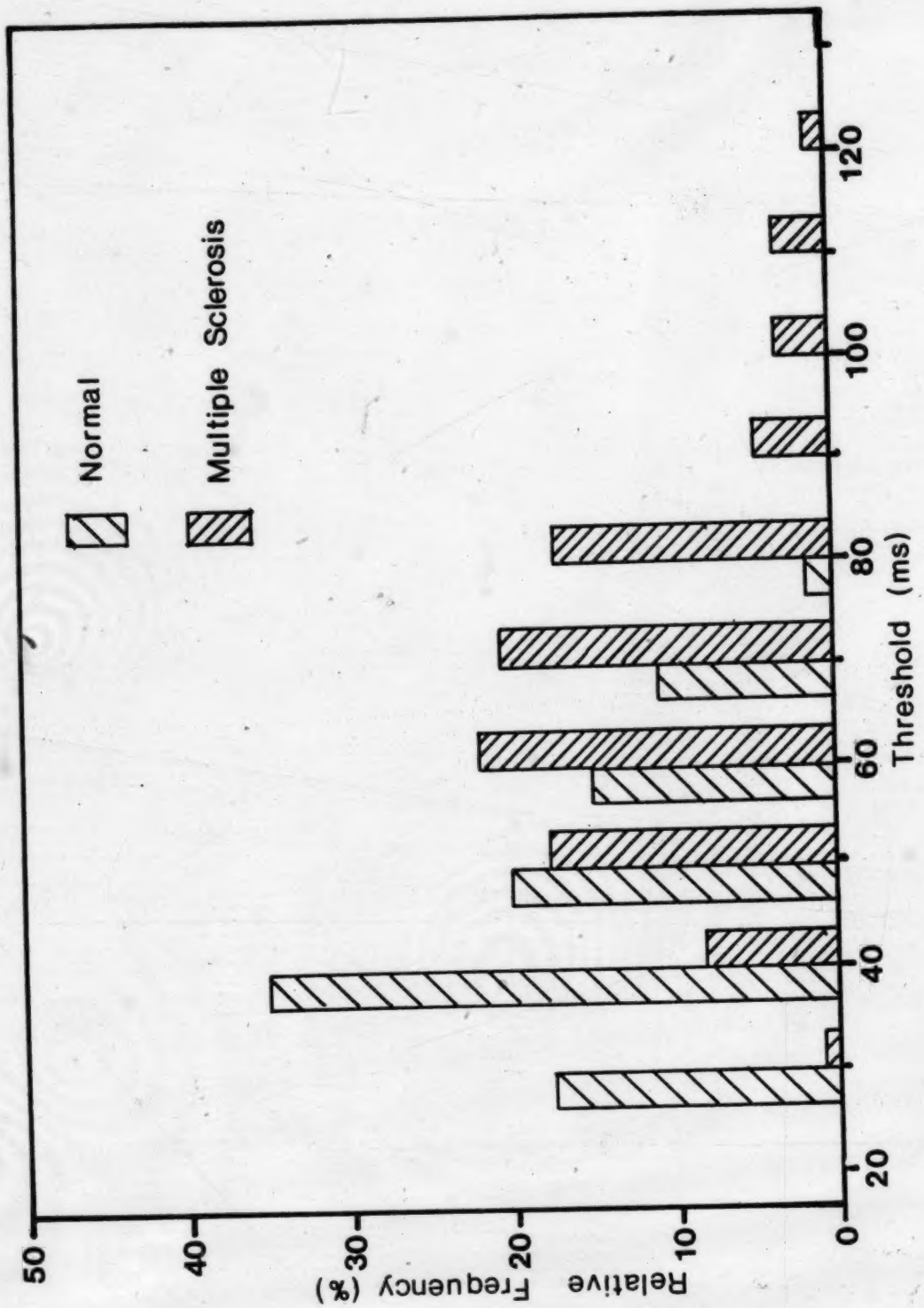

Normal
Multiple Sclerosis
Relative Frequency (%)
0
10
20
30
40
50
20
40
60
80
100
120
Threshold (ms)

Figure 26. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-bound task for normal eyes and eyes of patients with multiple sclerosis. Each eye contributed five thresholds: one from each location in the display.

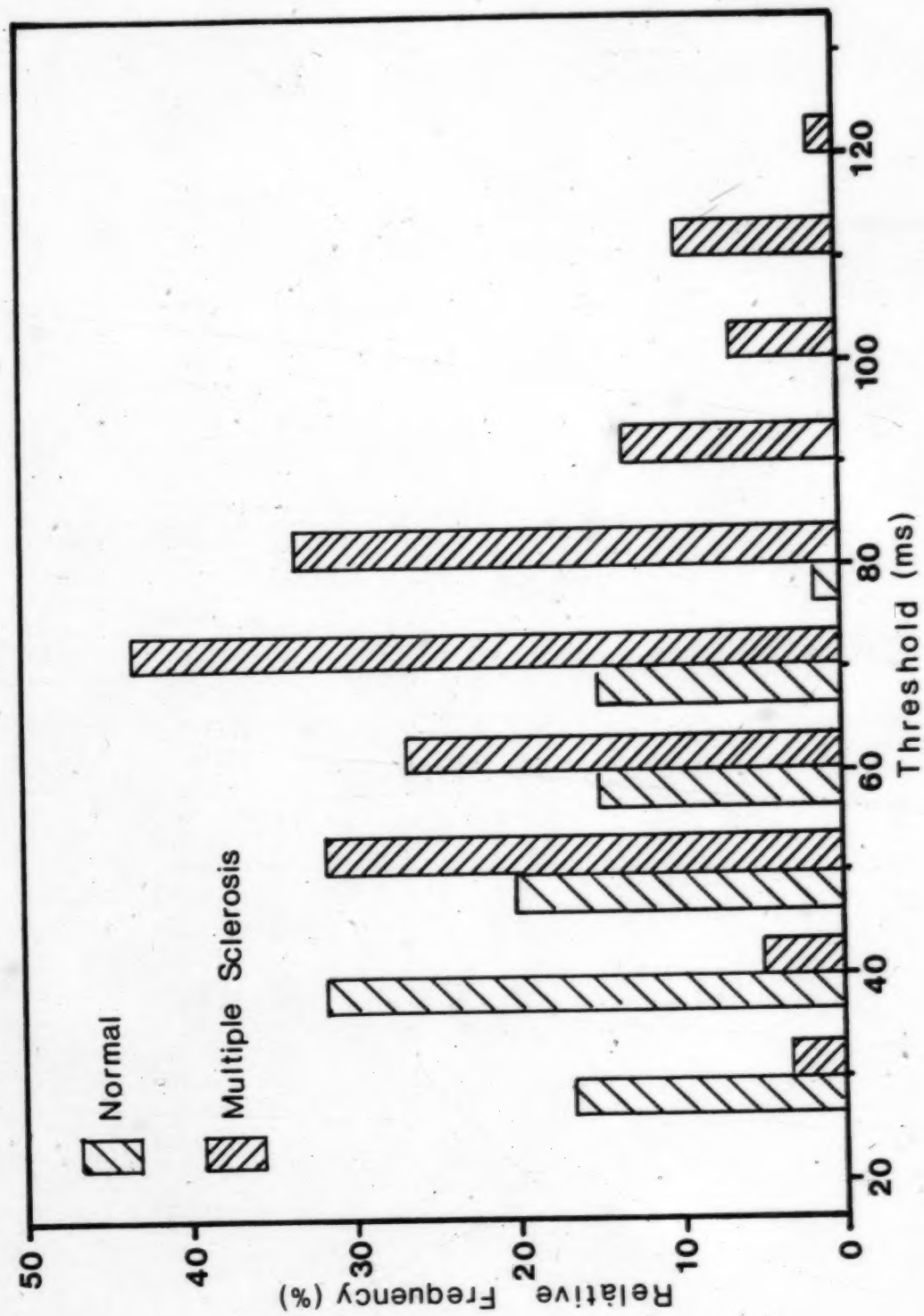
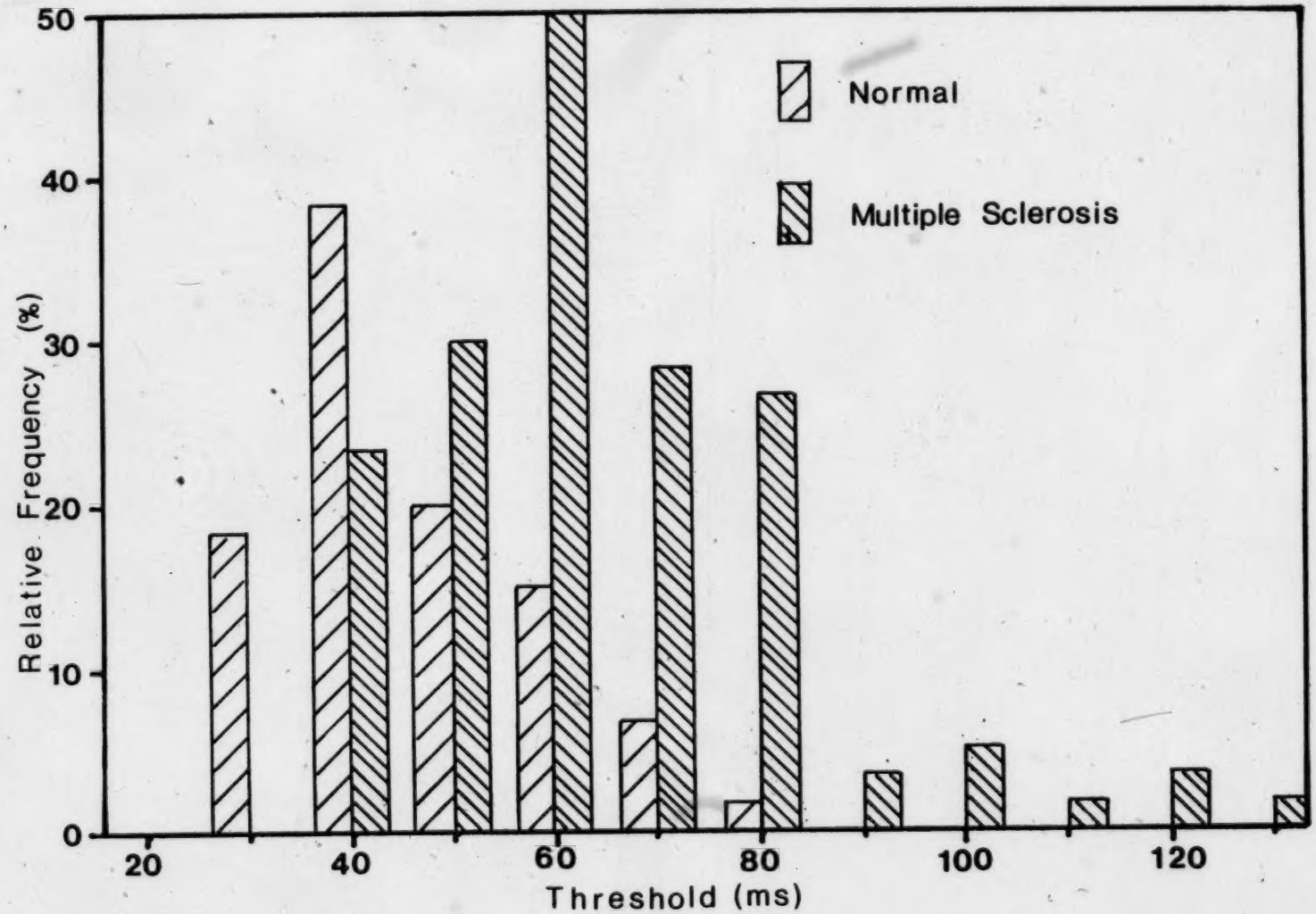

Normal
Multiple Sclerosis
Relative Frequency (%)
0
10
20
30
40
50
20
40
60
80
100
120
Threshold (ms)

Figure 27. Histograms showing the relative frequency of two-pulse resolution thresholds in the position-free task for normal eyes and eyes of patients with multiple sclerosis. Each eye contributed five thresholds: one from each location in the display.


50
40
30
20
10
0
Relative Frequency (%)
Normal
Multiple Sclerosis
20
40
60
80
100
120
Threshold (ms)

reported by Glavin et al. (1976, 1977) and suggests that the present technique can be regarded as a valid measure of two-pulse resolution thresholds.

Experiment 5

It should be evident that an abnormal two-pulse resolution threshold does not specify the nature of the underlying disorder. Without additional information it is impossible to know whether the cause of the temporal impairment is multiple sclerosis, glaucoma, or some other disease. As luck would have it, in the course of the present investigation one seemingly normal observer (JRT) was found to have abnormal results. An examination of his medical history did not reveal any possible causes for the deficits.

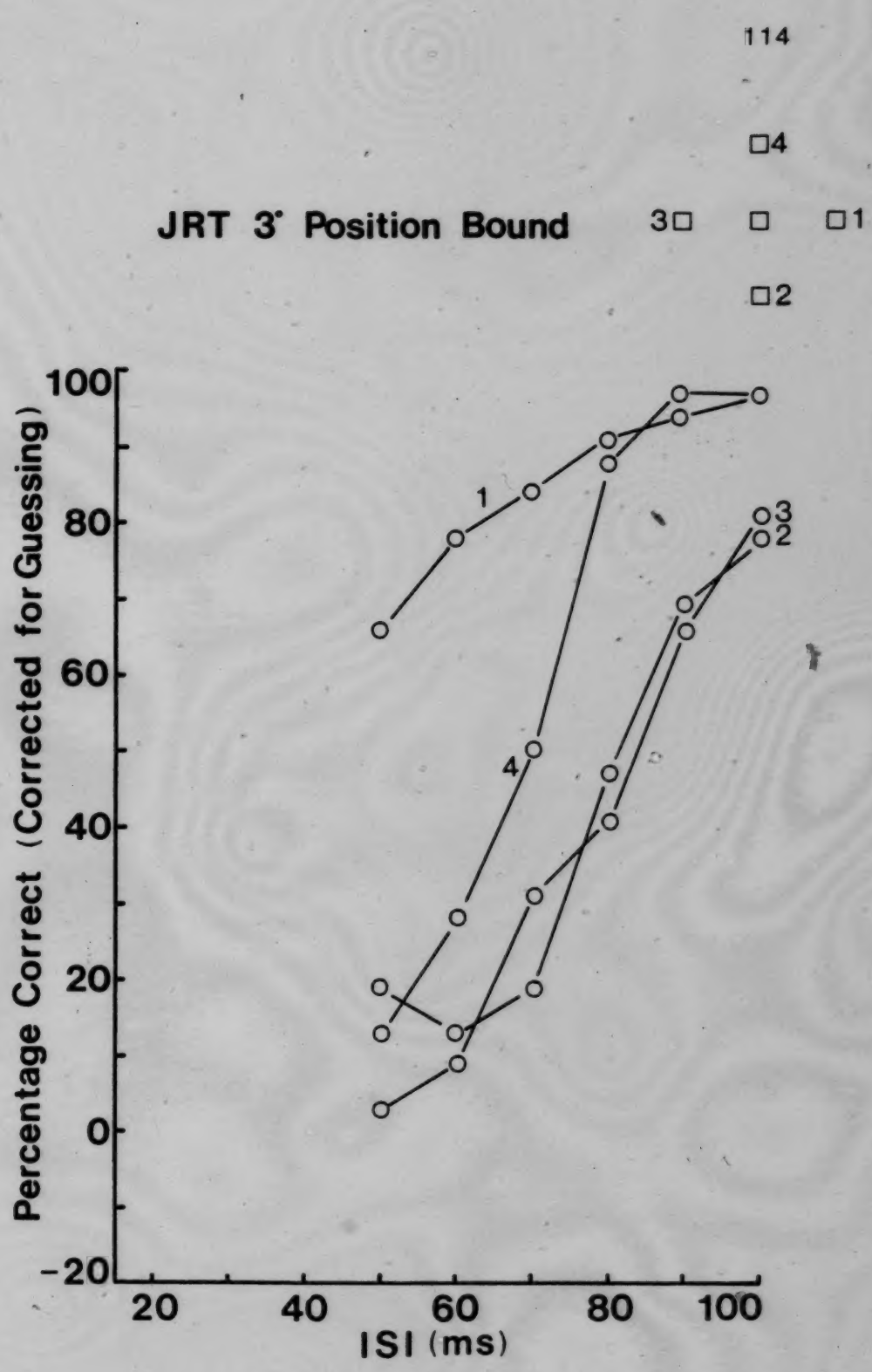
JRT served in Experiment 1. Method, display and procedures are described therein. JRT was 56 years old. His left eye was tested. It had good visual acuity (6/6), no perimetric field defects, normal pressure and a normal optic nerve head. His right eye had suffered an attack of closed angle glaucoma.

Results

Figure 28 shows results for observer JRT on the position-bound task. The position-free task yielded a similar pattern. Compare Figure 28 with Figures 9 through 13. Note the similarity between JRT's results and those of glaucomatous observers MT and AG. JRT required longer interpulse intervals to attain the same level of performance as control observers VDL and JMF, and showed the same dispersion amongst the curves representing performance at different locations in the display. Undeniably, his results belong with the glaucomatous group, yet his medical history belongs with the control observers.

It cannot be argued that the impairment in JRT's left eye is related to the closed angle glaucoma he suffered in the right eye. Closed angle glaucoma is a mechanical disorder of the eye where the sole cause of elevated intraocular pressure is the apposition of the iris to the trabechular meshwork. When the angle is open IOP is normal (Simmons and Dallow, 1984). There is no evidence that JRT had closed angle glaucoma in his left eye, and thus there is no reason to suspect glaucomatous damage.

Figure 28. Percentage of correct responses for observer JRT separately at each of the four outer display locations at an eccentricity of 3 degrees.


JRT 3° Position Bound
4
3
1
2
Percentage Correct (Corrected for Guessing)
100
80
60
40
20
0
-20
20
40
60
80
100
ISI (ms)
1
4
3
2

Conclusions

Elevated intraocular pressure is an important risk factor for developing damage to the optic nerve and for producing visual defects. However, not all eyes with elevated IOP develop glaucoma. When intraocular pressure is below 23 mm Hg about 3% of the eyes develop field defects. This rate increases steadily until at pressures over 30 mm Hg it is about 41% (Phelps, 1980; David, Livingston & Luntz, 1977). Furthermore, it is difficult to predict which patients will remain ocular hypertensive and which will become glaucomatous. Consequently, in managing patients with elevated IOP one is always faced with the question: when should treatment be initiated? Treating everyone with slight pressure elevation is unnecessary, but how can those patients who will progress to develop glaucoma be identified? This question has led to great interest in the description of early psychophysical abnormalities and other early signs of damage in patients with elevated intraocular pressure. It is hoped that this information might permit a more accurate assessment of the risk factors for developing glaucoma.

In this vein, the present work examined the diagnostic value of a two-pulse resolution task. The results were encouraging. Most patients who already had glaucoma were impaired at temporal resolution. But also, a certain percentage of ocular hypertensive patients had prolonged two-pulse thresholds. It remains to be seen whether these are the patients who will develop field defects.

With the exception of color vision losses (Drance and Lakowski, 1983), the prognostic value of most psychophysical tests is still unknown. There is a similar lack of information about the correlation amongst various psychophysical tests or about the probability of a patient showing deficits on more than one test. The area of glaucoma research is ripe for a longitudinal study of prognostic indicators of glaucoma. Such a study might examine the incidence of deficits on a set of psychophysical tests in a group of patients with elevated intraocular pressure and, after a number of years, assess which patients have developed glaucoma. A study like this would be very valuable and might permit the development of a battery of psychophysical tests which could identify those patients who require early intensive therapy. Of course, in the absence of this information it is impossible to evaluate the diagnostic merit of the two-pulse technique as compared to other techniques.

Another line of psychophysical research might seek to provide a better understanding of the disease process in glaucoma by identifying aspects of visual function which are not affected by the disorder. One example of this is given in the present dissertation: despite an overall difference in performance between position-bound and position-free tasks, the tasks did not discriminate between normal and clinical samples. This is consistent with the notion that the underlying processes that are responsible for the overall difference may be located at cortical levels (Wilson and Singer, 1981) and that they are unaffected by glaucoma.

Masking is another technique which may be particularly well suited for distinguishing aspects of visual function which are affected by glaucoma from those which are unaffected. Masking involves the presentation of a target and a mask in close temporal succession. The mask is displayed to the same retinal location as the target, and can either preceed or follow the target. Typically, the mask reduces the perceptability of the target. Masking effects can be subdivided into two broad categories: masking by "integration" where the mask and target fuse into one percept, and masking by "interruption" where the mask replaces the percept of the target. It has been suggested

(Scheerer, 1973) that masking is due to integration at stimulus onset assynchronies (SOAs) of less than about 150 ms, while at longer SOAs it is due to interruption. Furthermore, integration-type masking is believed to occur at relatively peripheral levels in the visual system, while interruption-type masking is believed to occur at relatively central levels. Given the pathophysiology of glaucoma, we might expect differences in masking effects to emerge between clinical and normal samples in integration-type masking, that is at SOAs below, but not above, about 150 ms.

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Appendix A

Percentage Correct Adjusted for Chance
JMF - Position Bound

2 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	-18.8	-3.1	71.9	93.8	100.0
Lower	40.6	53.1	84.4	87.5	96.9
Left	-9.4	3.1	37.5	87.5	100.0
Upper	3.1	40.6	84.4	96.9	100.0
Centre	-18.8	0.0	56.3	90.6	90.6
RLLUC	-0.6	18.8	66.9	91.3	97.5
RLLU	3.9	23.4	69.5	91.4	99.2

3 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	-6.3	21.9	71.9	100.0	100.0
Lower	31.3	71.9	81.3	93.8	96.9
Left	-9.4	37.5	75.0	93.8	93.8
Upper	3.1	28.1	62.5	93.8	96.9
Centre	0.0	34.4	65.6	90.6	100.0
RLLUC	3.8	38.8	71.3	94.4	97.5
RLLU	4.7	39.8	72.7	95.3	96.9

4 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	-12.5	12.5	56.3	93.8	90.6
Lower	18.8	59.4	68.8	93.8	90.6
Left	-6.3	34.4	87.5	93.8	100.0
Upper	-9.4	-6.3	21.9	56.3	75.0
Centre	12.5	31.3	75.0	100.0	100.0
RLLUC	0.6	26.3	61.9	87.5	91.3
RLLU	-2.3	25.0	58.6	84.4	89.1

Averaged across eccentricities: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	-12.5	10.4	66.7	95.8	96.9
Lower	30.2	61.5	78.1	91.7	94.8
Left	-8.3	25.0	66.7	91.7	97.9
Upper	-1.0	20.8	56.3	82.3	90.6
Centre	-2.1	21.9	65.6	93.8	96.9

Percentage Correct Adjusted for Chance
JMF - Position Free

2 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	25.0	-25.0	55.0	90.0	95.0
Lower	5.0	0.0	25.0	90.0	90.0
Left	10.0	-10.0	60.0	75.0	95.0
Upper	-30.0	-5.0	40.0	85.0	95.0
Centre	15.0	0.0	60.0	90.0	95.0
RLLUC	5.0	-8.0	48.0	86.0	94.0
RLLU	2.5	-10.0	45.0	85.0	93.8

3 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	15.0	10.0	55.0	85.0	100.0
Lower	-10.0	15.0	20.0	75.0	80.0
Left	25.0	15.0	75.0	95.0	95.0
Upper	5.0	0.0	35.0	85.0	100.0
Centre	-5.0	-20.0	60.0	85.0	95.0
RLLUC	6.0	4.0	49.0	85.0	94.0
RLLU	8.8	10.0	46.3	85.0	93.8

4 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	50.0
Right	-5.0	40.0	85.0	95.0	100.0
Lower	10.0	25.0	35.0	65.0	85.0
Left	-15.0	40.0	55.0	90.0	100.0
Upper	-15.0	0.0	15.0	30.0	75.0
Centre	15.0	15.0	50.0	85.0	90.0
RLLUC	-2.0	24.0	48.0	73.0	90.0
RLLU	-6.3	26.3	47.5	70.0	90.0

Averaged across eccentricities: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	11.7	8.3	65.0	90.0	98.3
Lower	1.7	13.3	26.7	76.7	85.0
Left	6.7	15.0	63.3	86.7	96.7
Upper	-13.3	-1.7	30.0	66.7	90.0
Centre	8.3	-1.7	56.7	86.7	93.3

Percentage Correct Adjusted for Chance
VDL - Position Bound

2 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	31.3	59.4	81.3	90.6	87.5
Lower	9.4	21.9	59.4	90.6	87.5
Left	-3.1	37.5	81.3	100.0	100.0
Upper	9.4	40.6	68.8	93.8	100.0
Centre	-9.4	46.9	96.9	93.8	100.0
RLLUC	7.5	41.3	77.5	93.8	95.0
RLLU	11.7	39.8	72.7	93.8	93.8

3 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	0.0	59.4	90.6	96.9	100.0
Lower	-6.3	18.8	53.1	65.6	90.6
Left	-6.3	25.0	59.4	96.9	100.0
Upper	12.5	40.6	65.6	87.5	100.0
Centre	-15.6	65.6	96.9	96.9	93.8
RLLUC	-3.1	41.9	73.1	88.8	96.9
RLLU	0.0	35.9	67.2	86.7	97.7

4 degrees: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	18.8	28.1	81.3	96.9	96.9
Lower	3.1	-3.1	15.6	18.8	46.9
Left	12.5	28.1	81.3	96.9	100.0
Upper	15.6	34.4	34.4	71.9	90.6
Centre	-12.5	28.1	87.5	93.8	90.6
RLLUC	7.5	23.1	60.0	75.6	85.0
RLLU	12.5	21.9	53.1	71.1	83.6

Averaged across eccentricities: ISI (msec)

	30.0	40.0	50.0	60.0	70.0
Right	16.7	49.0	84.4	94.8	94.8
Lower	2.1	12.5	42.7	58.3	75.0
Left	1.0	30.2	74.0	97.9	100.0
Upper	12.5	38.5	56.3	84.4	96.9
Centre	-12.5	46.9	93.8	94.8	94.8
RLLUC	4.0	35.4	70.2	86.0	92.3
RLLU	8.1	32.6	64.3	83.9	91.7

Percentage Correct Adjusted for Chance
VDL - Position Free

2 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	0.0	20.0	85.0	90.0	100.0
Lower	-20.0	10.0	25.0	80.0	85.0
Left	-5.0	35.0	50.0	75.0	100.0
Upper	0.0	-5.0	50.0	95.0	100.0
Centre	5.0	30.0	60.0	100.0	100.0
RLLUC	-4.0	18.0	54.0	88.0	97.0
RLLU	-6.3	15.0	52.5	85.0	96.3

3 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	5.0	15.0	50.0	90.0	100.0
Lower	20.0	20.0	10.0	50.0	95.0
Left	-15.0	20.0	50.0	80.0	100.0
Upper	5.0	25.0	20.0	55.0	90.0
Centre	5.0	30.0	60.0	100.0	100.0
RLLUC	4.0	22.0	38.0	75.0	97.0
RLLU	3.8	20.0	32.5	68.8	96.3

4 degrees: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	0.0	25.0	55.0	95.0	100.0
Lower	0.0	15.0	10.0	10.0	70.0
Left	0.0	20.0	25.0	70.0	100.0
Upper	0.0	0.0	20.0	45.0	45.0
Centre	-10.0	-10.0	70.0	90.0	100.0
RLLUC	-2.0	10.0	36.0	62.0	83.0
RLLU	0.0	15.0	27.5	55.0	78.8

Averaged across eccentricities: ISI (msec)

	20.0	30.0	40.0	50.0	60.0
Right	1.7	20.0	63.3	91.7	100.0
Lower	0.0	15.0	15.0	46.7	83.3
Left	-6.7	25.0	41.7	75.0	100.0
Upper	1.7	6.7	30.0	65.0	78.3
Centre	0.0	16.7	63.3	96.7	100.0
RLLUC	-0.7	16.7	42.7	75.0	92.3
RLLU	-0.8	16.7	37.5	69.6	90.4

Percentage Correct Adjusted for Chance
WS - Position Bound

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0
right	6.3	43.8	90.6	90.6	100.0		
lower			31.3	62.5	78.1	87.5	100.0
left	12.5	25.0	65.6	81.3	96.9		
upper	21.9	81.3	81.3	96.9	100.0		
center	-3.1	25.0	71.9	87.5	100.0		
rlluc	9.4	43.8	68.1	83.8	95.0	87.5	100.0
rllu	13.5	50.0	67.2	82.8	93.8	87.5	100.0

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0
right	-3.1	56.3	71.9	93.8	100.0		
lower			25.0	78.1	90.6	96.9	100.0
left	6.3	25.0	53.1	81.3	93.8		
upper	0.0	43.8	53.1	87.5	96.9		
center	6.3	21.9	87.5	100.0	100.0		
rlluc	2.3	36.7	58.1	88.1	96.3	96.9	100.0
rllu	1.0	41.7	50.8	85.2	95.3	96.9	100.0

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0
right		9.4	68.8	96.9	93.8	100.0	
lower			25.0	68.8	96.9	87.5	96.9
left		25.0	43.8	75.0	93.8	90.6	
upper		21.9	40.6	59.4	84.4	87.5	
center		56.3	93.8	81.3	96.9	100.0	
rlluc		28.1	54.4	76.3	93.1	93.1	96.9
rllu		18.8	44.5	75.0	92.2	91.4	96.9

Averaged across eccentricities: ISI (msec)

	50.0	60.0	70.0
right	77.1	93.8	97.9
lower	27.1	69.8	88.5
left	54.2	79.2	94.8
upper	58.3	81.3	93.8
center	84.4	89.6	99.0
rlluc	60.2	82.7	94.8
rllu	54.2	81.0	93.8

Percentage Correct Adjusted for Chance
WS - Position Free

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	25.0	80.0	90.0	100.0	100.0	
lower		15.0	70.0	95.0	100.0	95.0
left	15.0	40.0	75.0	95.0	100.0	
upper	-15.0	95.0	100.0	95.0	95.0	
center	20.0	50.0	85.0	100.0	95.0	
rlluc	11.3	56.0	84.0	97.0	98.0	95.0
rllu	8.3	57.5	83.8	96.3	98.8	95.0

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	35.0	55.0	95.0	100.0	100.0	
lower		45.0	65.0	75.0	85.0	100.0
left	15.0	35.0	85.0	85.0	100.0	
upper	30.0	85.0	95.0	100.0	100.0	
center	40.0	30.0	100.0	90.0	90.0	
rlluc	30.0	50.0	88.0	90.0	95.0	100.0
rllu	26.7	55.0	85.0	90.0	96.3	100.0

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	20.0	70.0	70.0	100.0	100.0	
lower		25.0	80.0	65.0	90.0	95.0
left	50.0	50.0	75.0	85.0	95.0	
upper	15.0	35.0	65.0	85.0	85.0	
center	15.0	80.0	100.0	100.0	100.0	
rlluc	25.0	52.0	78.0	87.0	94.0	95.0
rllu	28.3	45.0	72.5	83.8	92.5	95.0

Averaged across eccentricities: ISI (msec)

	40.0	50.0	60.0	70.0
right	68.3	85.0	100.0	100.0
lower	28.3	71.7	78.3	91.7
left	41.7	78.3	88.3	98.3
upper	71.7	86.7	93.3	93.3
center	53.3	95.0	96.7	95.0
rlluc	52.7	83.3	91.3	95.7
rllu	52.5	80.4	90.0	95.8

Percentage Correct Adjusted for Chance
AG - Position Bound

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right		21.9	50.0	84.4	93.8	100.0	96.9	100.0
lower		-21.9	0.0	31.3	59.4	65.6	68.8	93.8
left		9.4	40.6	81.3	93.8	100.0	100.0	100.0
upper		3.1	28.1	81.3	96.9	100.0	100.0	100.0
center		34.4	43.8	81.3	96.9	96.9	100.0	100.0
rlluc		9.4	32.5	71.9	88.1	92.5	93.1	98.8
rllu		3.1	29.7	69.5	85.9	91.4	91.4	98.4

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right		25.0	34.4	65.6	96.9	100.0	96.9	100.0
lower		-15.6	-6.3	15.6	21.9	25.0	71.9	71.9
left		21.9	40.6	65.6	93.8	100.0	96.9	96.9
upper		-3.1	21.9	53.1	90.6	100.0	100.0	100.0
center		18.8	59.4	96.9	96.9	96.9	100.0	100.0
rlluc		9.4	30.0	59.4	80.0	84.4	93.1	93.8
rllu		7.0	22.7	50.0	75.8	81.3	91.4	92.2

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right		6.3	15.6	43.8	84.4	100.0	96.9	96.9
lower		-18.8	-25.0	-9.4	-12.5	12.5	28.1	53.1
left		31.3	56.3	71.9	87.5	100.0	100.0	100.0
upper		-12.5	6.3	25.0	56.3	78.1	87.5	90.6
center		0.0	84.4	90.6	100.0	100.0	100.0	93.8
rlluc		1.3	27.5	44.4	63.1	78.1	82.5	86.9
rllu		1.6	13.3	32.8	53.9	72.7	78.1	85.2

Average across eccentricities: ISI (msec)

	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right	17.7	33.3	64.6	91.7	100.0	96.9	99.0
lower	-18.8	-10.4	12.5	22.9	34.4	56.3	72.9
left	20.8	45.8	72.9	91.7	100.0	99.0	99.0
upper	-4.2	18.8	53.1	81.3	92.7	95.8	96.9
cente	17.7	62.5	89.6	97.9	97.9	100.0	97.9

Percentage Correct Adjusted for Chance
AG - Position Free

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	-10.0	45.0	60.0	100.0	95.0	100.0
lower	40.0	30.0	40.0	35.0	55.0	75.0
left	5.0	5.0	10.0	90.0	90.0	100.0
upper	10.0	10.0	70.0	80.0	85.0	100.0
center	20.0	5.0	90.0	95.0	95.0	95.0
rlluc	13.0	19.0	54.0	80.0	84.0	94.0
rllu	11.3	22.5	45.0	76.3	81.3	93.8

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	-5.0	30.0	55.0	85.0	95.0	95.0
lower	25.0	30.0	15.0	40.0	55.0	50.0
left	15.0	20.0	70.0	75.0	90.0	95.0
upper	-15.0	35.0	45.0	65.0	80.0	95.0
center	-10.0	40.0	85.0	95.0	100.0	95.0
rlluc	2.0	31.0	54.0	72.0	84.0	86.0
rllu	5.0	28.8	46.3	66.3	80.0	83.8

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0
right	-20.0	20.0	40.0	50.0	95.0	95.0
lower	-5.0	20.0	0.0	15.0	25.0	35.0
left	0.0	60.0	70.0	75.0	95.0	95.0
upper	20.0	10.0	30.0	45.0	65.0	80.0
center	0.0	35.0	80.0	100.0	100.0	100.0
rlluc	-1.0	29.0	44.0	57.0	76.0	81.0
rllu	-1.3	27.5	35.0	46.3	70.0	76.3

Average across eccentricities: ISI (msec)

	40.0	50.0	60.0	70.0	80.0
right	31.7	51.7	78.3	95.0	96.7
lower	26.7	18.3	30.0	45.0	53.3
left	28.3	50.0	80.0	91.7	96.7
upper	18.3	48.3	63.3	76.7	91.7
center	26.7	85.0	96.7	98.3	96.7

Percentage Correct Adjusted for Chance
MT - Position Bound

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right		-15.6	6.3	37.5	81.3	93.8		
lower				6.3	43.8	68.8	84.4	100.0
left		-12.5	-6.3	15.6	50.0	93.8		
upper		-15.6	6.3	25.0	71.9	93.8		
center		-21.9	-12.5	18.8	75.0	96.9		
rlluc		-16.4	-1.6	20.6	64.4	89.4	84.4	100.0
rllu		-14.6	2.1	21.1	61.7	87.5	84.4	100.0

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right	0.0	12.5	34.4	50.0	81.3	87.5		
lower			-15.6	6.3	40.6	65.6	75.0	90.6
left		-21.9	-15.6	3.1	31.3	68.8	78.1	
upper			3.1	-9.4	28.1	68.8	78.1	90.6
center		-9.4	0.0	28.1	50.0	78.1	96.9	
rlluc	0.0	-6.3	1.3	15.6	46.3	73.8	82.0	90.6
rllu	0.0	-4.7	1.6	12.5	45.3	72.7	77.1	90.6

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right	15.6	6.3	15.6	31.3	84.4	84.4		
lower			-12.5	6.3	-3.1	43.8	53.1	68.8
left		-15.6	-9.4	3.1	43.8	84.4	90.6	
upper			-3.1	0.0	15.6	56.3	53.1	68.8
center		0.0	3.1	28.1	56.3	65.6	90.6	
rlluc	15.6	-3.1	-1.3	13.8	39.4	66.9	71.9	68.8
rllu	15.6	-4.7	-2.3	10.2	35.2	67.2	65.6	68.8

Averaged across eccentricities: ISI (msec)

	60.0	70.0	80.0
right	39.6	82.3	88.5
lower	6.3	27.1	59.4
left	7.3	41.7	82.3
upper	5.2	38.5	72.9
center	25.0	60.4	80.2

Percentage Correct Adjusted for Chance
MT - Position Free

2 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right		15.0	20.0	60.0	100.0	100.0		
lower				30.0	45.0	85.0	75.0	90.0
left		10.0	10.0	40.0	65.0	90.0		
upper		25.0	15.0	70.0	95.0	90.0		
center		5.0	-5.0	45.0	55.0	85.0		
rlluc		13.8	10.0	49.0	72.0	90.0	75.0	90.0
rllu		16.7	15.0	50.0	76.3	91.3	75.0	90.0

3 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right	10.0	-15.0	50.0	80.0	90.0	100.0		
lower			0.0	5.0	45.0	80.0	65.0	80.0
left		30.0	0.0	30.0	55.0	80.0	95.0	
upper			10.0	60.0	25.0	90.0	90.0	100.0
center		-20.0	0.0	30.0	70.0	95.0	85.0	
rlluc	10.0	-1.7	12.0	41.0	57.0	89.0	83.8	90.0
rllu	10.0	7.5	15.0	43.8	53.8	87.5	83.3	90.0

4 degrees: ISI(msec)

	30.0	40.0	50.0	60.0	70.0	80.0	90.0	100.0
right	15.0	-5.0	10.0	85.0	90.0	90.0		
lower			15.0	25.0	-10.0	15.0	65.0	55.0
left		-10.0	5.0	30.0	65.0	70.0	100.0	
upper			-20.0	25.0	60.0	50.0	70.0	70.0
center		-5.0	20.0	40.0	65.0	65.0	85.0	
rlluc	15.0	-6.7	6.0	41.0	54.0	58.0	80.0	62.5
rllu	15.0	-7.5	2.5	41.3	51.3	56.3	78.3	62.5

Averaged across eccentricities: ISI (msec)

	60.0	70.0	80.0
right	75.0	93.3	96.7
lower	20.0	26.7	60.0
left	33.3	61.7	80.0
upper	51.7	60.0	76.7
center	38.3	63.3	81.7